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TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  4  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08  Gene Names now available in BIOSIS
 NEWS  7  Mar 22  TOXLIT no longer available
 NEWS  8  Mar 22  TRCTHERMO no longer available
 NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 10  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14  Apr 09  ZDB will be removed from STN
 NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *



FILE 'HOME' ENTERED AT 12:01:19 ON 13 MAY 2002

=> fil reg
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY    SESSION
FULL ESTIMATED COST                             0.21       0.21
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FILE 'REGISTRY' ENTERED AT 12:01:28 ON 13 MAY 2002
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STRUCTURE FILE UPDATES:   12 MAY 2002  HIGHEST RN 414355-21-8
DICTIONARY FILE UPDATES:  12 MAY 2002  HIGHEST RN 414355-21-8

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

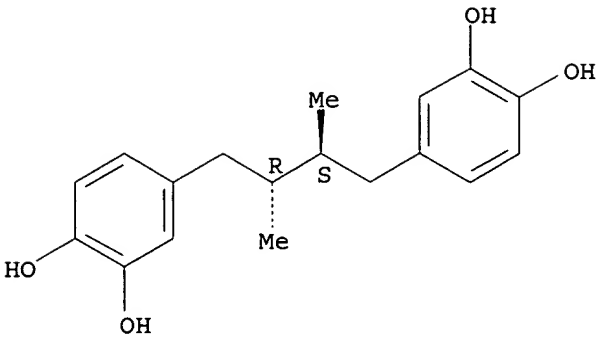
=> e nordihydroguaiaretic acid
E1            1     NORDIHYDROFUMARILINE/BI
E2            2     NORDIHYDROGUAIARETIC/BI
E3            0 --> NORDIHYDROGUAIARETIC ACID/BI
E4            6     NORDIHYDROISO/BI
E5            2     NORDIHYDROISOACRONYCINE/BI
E6            2     NORDIHYDROISOCODEINE/BI
E7            2     NORDIHYDROISOMORPHINE/BI
E8            3     NORDIHYDROL/BI
E9            1     NORDIHYDROLANOSTER/BI
E10           1     NORDIHYDROLANOSTEROL/BI
E11           1     NORDIHYDROLAPA/BI
E12           1     NORDIHYDROLAPACHEN/BI

=> s nordihydroguaiaretic
L1            2 NORDIHYDROGUAIARETIC

=> d tot

L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2002 ACS
RN   27686-84-6  REGISTRY
CN   1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-, (R*,S*)- (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Pyrocatechol, 4,4'-(2,3-dimethyltetramethylene)di-, meso- (8CI)
OTHER NAMES:
CN   CHX 100
CN   Masoprocol
CN   meso-NDGA
CN   meso-Nordihydroguaiaretic acid
FS   STEREOSEARCH
DR   334707-72-1
MF   C18 H22 O4
CI   COM
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, CA, CAPLUS, CASREACT, CBNB, CHEMLIST, CIN, DDFU, DIOGENES,
       DRUGNL, DRUGU, DRUGUPDATES, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*,
       NAPRALERT, PHAR, PROMT, TOXCENTER, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

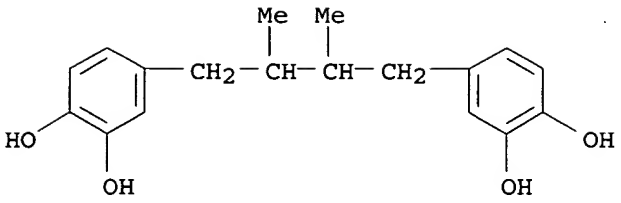
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

33 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 500-38-9 REGISTRY
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrocatechol, 4,4'-(2,3-dimethyltetramethylene)di- (8CI)
OTHER NAMES:
CN .beta.,.gamma.-Dimethyl-.alpha.,.delta.-bis(3,4-dihydroxyphenyl)butane
CN 1,4-Bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane
CN 4,4'-(2,3-Dimethyl-1,4-butanediyl)bis(pyrocatechol)
CN 4,4'-(2,3-Dimethyltetramethylene)dipyrocatechol
CN Butane, 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethyl-
CN Dihydronorguaiaretic acid
CN Dinorguaiaretic acid, dihydro-
CN NDGA
CN **Nordihydroguaiaretic acid**
CN Norguaiaretic acid, dihydro-
FS 3D CONCORD
DR 1413-68-9
MF C18 H22 O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXCENTER, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1093 REFERENCES IN FILE CA (1967 TO DATE)
19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1096 REFERENCES IN FILE CAPLUS (1967 TO DATE)
17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> sel rn name l1 2
E13 THROUGH E23 ASSIGNED

=> del sel
DELETE ALL E# DEFINITIONS? (Y)/N:y

=> sel rn name l1 2
E1 THROUGH E11 ASSIGNED

=> fil medli hcapl biosis uspatful
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.00	9.21

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FILE 'USPATFULL' ENTERED AT 12:03:00 ON 13 MAY 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s e1-11
2 FILES SEARCHED...
3 FILES SEARCHED...
L2 7634 (".BETA.,.GAMMA.-DIMETHYL-.ALPHA.,.DELTA.-BIS(3,4-DIHYDROXYPHENYL)BUTANE"/BI OR "BUTANE, 1,4-BIS(3,4-DIHYDROXYPHENYL)-2,3-DIMETHYL-"/BI OR "DIHYDRONORGUAIARETIC ACID"/BI OR "DINORGUAIARETIC ACID, DIHYDRO-"/BI OR NDGA/BI OR "NORDIHYDROGUAIARETIC ACID"/BI OR "NORGUAIARETIC ACID, DIHYDRO-"/BI OR "1,4-BIS(3,4-DIHYDROXYPHENYL)-2,3-DIMETHYLBUTANE"/BI OR "4,4'-(2,3-DIMETHYL-1,4-BUTANEDIYL)BIS(PYROCATECHOL)"/BI OR "4,4'-(2,3-DIMETHYLTETRAMETHYLENE)DIPYROCATECHOL"/BI OR 500-38-9/BI)

=> s lipoxygenase
L3 39733 LIPOXYGENASE

=> s l2 and l3

```
L4        4244 L2 AND L3

=> s l2 (s) l3
L5        3540 L2 (S) L3

=> s inhibit? or reduc? or decreas?
   3 FILES SEARCHED...
L6    11245322 INHIBIT? OR REDUC? OR DECREAS?

=> s l5 (S) l6
L7        3420 L5 (S) L6

=> d scan

L7    3420 ANSWERS   HCAPLUS  COPYRIGHT 2002 ACS
CC    14-1 (Mammalian Pathological Biochemistry)
      Section cross-reference(s): 2, 7, 13
TI    Arachidonic and Linoleic Acid Metabolism in Mouse Intestinal Tissue:
      Evidence for Novel Lipoxygenase Activity
ST    arachidonic linoleic acid metab lipoxygenase cyclooxygenase intestine
      polyp
IT    Disease models
         (Min mouse; arachidonic and linoleic acid metab. and cyclooxygenase and
         lipoxygenases expression and activity in intestinal polyps and adjacent
         tissue Min mouse)
IT    Cell differentiation
      Transformation, neoplastic
         (arachidonic and linoleic acid metab. and cyclooxygenase and
         lipoxygenases expression and activity in intestinal polyps and adjacent
         tissue)
IT    Mouse
         (arachidonic and linoleic acid metab. and cyclooxygenase and
         lipoxygenases expression and activity in intestinal polyps and adjacent
         tissue of Min mouse)
IT    Intestine, neoplasm
         (colon, polyp; arachidonic and linoleic acid metab. and cyclooxygenase
         and lipoxygenases expression and activity in intestinal polyps and
         adjacent tissue)
IT    Intestine, neoplasm
         (colorectal; arachidonic and linoleic acid metab. and cyclooxygenase
         and lipoxygenases expression and activity in intestinal polyps and
         adjacent tissue)
IT    Intestine
         (epithelium; arachidonic and linoleic acid metab. and cyclooxygenase
         and lipoxygenases expression and activity in intestinal polyps and
         adjacent tissue)
IT    60-33-3, Linoleic Acid, biological studies   363-24-6, PGE2   506-32-1,
      Arachidonic acid   551-11-1, PGF2.alpha.   10075-11-3   10219-69-9
      29623-28-7   54232-59-6   54397-83-0   54739-30-9   54845-95-3,
      15(S)-Hydroxyeicosatetraenoic acid   63551-74-6, Lipoxygenase   73543-67-6
      80619-02-9, 5-Lipoxygenase   82391-43-3, 12(s)-Lipoxygenase   100900-72-9,
      8-Lipoxygenase   329900-75-6, Cyclooxygenase-2
      RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (arachidonic and linoleic acid metab. and cyclooxygenase and
         lipoxygenases expression and activity in intestinal polyps and adjacent
         tissue)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L7    3420 ANSWERS   HCAPLUS  COPYRIGHT 2002 ACS
CC    13-6 (Mammalian Biochemistry)
      Section cross-reference(s): 4, 6
```

TI Lipoxygenase May Be Involved in Cationic Liposome-Induced Macrophage Apoptosis
ST lipoxygenase reactive oxygen cationic liposome macrophage apoptosis
IT Liposomes
(cationic; involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis)
IT Apoptosis
Macrophage
(involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis)
IT Reactive oxygen species
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis)
IT Peroxidation
(lipid; involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis in relation to)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peroxidn.; involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis in relation to)
IT 7782-44-7D, Oxygen, reactive species
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis)
IT 506-32-1, Arachidonic acid 63551-74-6, Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(involvement of lipoxygenase in reactive oxygen species generation and cationic liposome-induced macrophage apoptosis)

L7 3420 ANSWERS HCAPLUS COPYRIGHT 2002 ACS
CC 1-12 (Pharmacology)
TI trans-10,cis-12-Conjugated Linoleic Acid Reduces Leptin Secretion from 3T3-L1 Adipocytes
ST linoleate conjugate leptin mRNA adipocyte body wt
IT Adipose tissue
(adipocyte; trans-10, cis-12-conjugated linoleic acid reduces leptin secretion from 3T3-L1 adipocytes)
IT Body weight
(trans-10, cis-12-conjugated linoleic acid reduces leptin secretion from 3T3-L1 adipocytes)
IT 169494-85-3, Leptin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mRNA expression; trans-10, cis-12-conjugated linoleic acid reduces leptin secretion from 3T3-L1 adipocytes)
IT 500-38-9, Nordihydroguaiaretic acid 2420-56-6, 10-trans,12-cis-Linoleic acid 30643-68-6, Nonadecadienoic acid 74772-77-3, Ciglitazone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(trans-10, cis-12-conjugated linoleic acid reduces leptin secretion from 3T3-L1 adipocytes)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s weight or obes? or antiobes?
L8 3345044 WEIGHT OR OBES? OR ANTIOBES?

=> s l8 (S) l7
L9 28 L8 (S) L7

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 17 DUP REM L9 (11 DUPLICATES REMOVED)

=> d ibib abs kwic 12-17

L10 ANSWER 12 OF 17 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 87111562 MEDLINE
DOCUMENT NUMBER: 87111562 PubMed ID: 3100723
TITLE: Arachidonic acid oxidation by brain and placenta preparations from normal and placental insufficient fetal rabbit.
AUTHOR: Goldin E; Harel S; Tomer A; Yavin E
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1987 Mar) 48 (3) 695-701. Journal code: JAV; 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198703
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870319

AB Cytosolic (100,000 g) fractions of fetal rabbit brain and placenta tissue convert [1-14C]arachidonic acid into several oxidation products identified with the **lipoxygenase** [12-hydroxyeicosatetraenoic acid (12-HETE) and 15-HETE] and cyclooxygenase [prostaglandin E2 (PGE2)] pathways. Formation of 12-HETE and 15-HETE by fetal brain is time-dependent, reaching a plateau after 40 min and is linear with protein concentration. An apparent affinity constant of 0.06 mM and a Vmax of 0.1 mumol/h/g wet **weight** are presumably responsible for the excessive accumulation of 12-HETE and 15-HETE in comparison to PGE2 (Km = 0.5 mM). The latter is synthesized by the placenta particulate fraction but almost exclusively by the brain cytosol. Compared to brain, the activity of the placenta tissue is exceedingly higher and in addition to 12-HETE and 15-HETE there is a substantial formation of 12-L-hydroxyheptadecatrienic acid. Formation of 12-HETE and 15-HETE at 21 days is as effective as at 31 days gestation and is strongly **inhibited** by **nordihydroguaiaretic acid** (93%), BW755c (99%), and AA861 (84%) but not by indomethacin. Placenta and brain tissues of intrauterine growth retarded fetuses after ligation of placental blood vessels fail to convert arachidonic acid into other eicosanoids. Loss of enzymatic activity also observed in normal tissue after prolonged storage cannot be restored by the addition of several SH agents, ascorbate, or ferric iron.

AB . . . (100,000 g) fractions of fetal rabbit brain and placenta tissue convert [1-14C]arachidonic acid into several oxidation products identified with the **lipoxygenase** [12-hydroxyeicosatetraenoic acid (12-HETE) and 15-HETE] and cyclooxygenase [prostaglandin E2 (PGE2)] pathways. Formation of 12-HETE and 15-HETE by fetal brain is. . . and is linear with protein concentration. An apparent affinity constant of 0.06 mM and a Vmax of 0.1 mumol/h/g wet **weight** are presumably responsible for the excessive accumulation of 12-HETE and 15-HETE in comparison to PGE2 (Km = 0.5 mM). The. . . acid. Formation of 12-HETE and 15-HETE at 21 days is as effective as at 31 days gestation and is strongly **inhibited** by **nordihydroguaiaretic acid** (93%), BW755c (99%), and AA861 (84%) but not by indomethacin. Placenta and brain tissues of intrauterine growth retarded fetuses after. . .

L10 ANSWER 13 OF 17 MEDLINE
ACCESSION NUMBER: 88006374 MEDLINE
DOCUMENT NUMBER: 88006374 PubMed ID: 2820876

TITLE: Poly L-histidine. A potent stimulator of superoxide generation in human blood leukocytes.
AUTHOR: Ginsburg I; Borinski R; Sadovnic M; Eilam Y; Rainsford K
CORPORATE SOURCE: Department of Oral Biology, Hebrew University-Hadassah School of Dental Medicine, Israel.
SOURCE: INFLAMMATION, (1987 Sep) 11 (3) 253-77.
Journal code: GM0; 7600105. ISSN: 0360-3997.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19871028

AB Poly-L-histidine (PHSTD) of molecular **weight** 26,000 induced the generation of large amounts of superoxide (O2-) and hydrogen peroxide (H2O2) in human neutrophils (PMNs). Despite its low solubility at neutral pH, PHSTD was bound very rapidly to the PMN surfaces. Maximal generation of O2- took place with 4-5 X 10(-6) M of PHSTD, starting after a lag of about 25 sec and proceeding for 15-17 min at a rate of 150 nmol/10(7) PMNs/min, suggesting that this polycation is one of the most potent stimulators of O2- generation known, PHSTD was found to be non-toxic for PMNs even at millimolar concentrations. Generation of O2- by PHSTD depended on extracellular calcium; it was **inhibited** by calcium channel blockers and by trifluoperazine, and it triggered a sharp rise in intracellular calcium as determined by the Quin 2 fluorescence technique. The generation of both O2- and H2O2 by PHSTD was partially **inhibited** by cytochalasin B or (CYB, CYE). On the other hand, CYB markedly enhanced the generation of both O2- and H2O2 following stimulation of PMNs either by PHSTD, polyarginine, histone, or by antibody-opsonized group A streptococci. Electron microscopic analysis and NBT **reduction** tests revealed that both PHSTD and PHSTD-opsonized streptococci were avidly phagocytosed by PMNs. Since CYB totally **inhibited** internalization of both PHSTD and the PHSTD-opsonized streptococci, it was suggested that these agents stimulated oxygen radical generation mainly on the leukocyte surfaces. Complexes (CX) formed between PHSTD and polyanethole sulfonate (a strong polyanion) or between histone and the polyanion mimicked immune CX in their ability to trigger the generation of large amounts of O2- which were **inhibited** by CYB. Generation of O2- and chemiluminescence either by PHSTD or by PHSTD-opsonized streptococci were markedly **inhibited** by poly-L-glutamate, suggesting that PHSTD acted as a cationic agent which interacted via electrostatic forces with some negatively charged sites in the leukocyte membrane. Generation of H2O2 by PHSTD was also markedly **inhibited** by deoxyglucose, KCN, DASA, as well as by the **lipoxygenase inhibitors nordihydroguaiaretic acid**, phenidone, and propylgallate. On the other hand, cyclooxygenase **inhibitors** such as aspirin, indomethacin, and piroxicam were inactive, suggesting that arachidonic acid metabolism via **lipoxygenase** pathway might have been involved in the activation by PHSTD of the NADPH oxidase in PMNs.(ABSTRACT TRUNCATED AT 400 WORDS)

AB Poly-L-histidine (PHSTD) of molecular **weight** 26,000 induced the generation of large amounts of superoxide (O2-) and hydrogen peroxide (H2O2) in human neutrophils (PMNs). Despite its. . . to be non-toxic for PMNs even at millimolar concentrations. Generation of O2- by PHSTD depended on extracellular calcium; it was **inhibited** by calcium channel blockers and by trifluoperazine, and it triggered a sharp rise in intracellular calcium as determined by the Quin 2 fluorescence technique. The generation of both O2- and H2O2 by PHSTD was partially **inhibited** by cytochalasin B or (CYB, CYE). On the other hand, CYB markedly enhanced the generation of both O2- and H2O2. . . following

stimulation of PMNs either by PHSTD, polyarginine, histone, or by antibody-opsonized group A streptococci. Electron microscopic analysis and NBT **reduction** tests revealed that both PHSTD and PHSTD-opsonized streptococci were avidly phagocytosed by PMNs. Since CYB totally **inhibited** internalization of both PHSTD and the PHSTD-opsonized streptococci, it was suggested that these agents stimulated oxygen radical generation mainly on. . . and the polyanion mimicked immune CX in their ability to trigger the generation of large amounts of O2- which were **inhibited** by CYB. Generation of O2- and chemiluminescence either by PHSTD or by PHSTD-opsonized streptococci were markedly **inhibited** by poly-L-glutamate, suggesting that PHSTD acted as a cationic agent which interacted via electrostatic forces with some negatively charged sites in the leukocyte membrane. Generation of H2O2 by PHSTD was also markedly **inhibited** by deoxyglucose, KCN, DASA, as well as by the **lipoxygenase inhibitors** **nordihydroguaiaretic acid**, phenidone, and propylgallate. On the other hand, cyclooxygenase **inhibitors** such as aspirin, indomethacin, and piroxicam were inactive, suggesting that arachidonic acid metabolism via **lipoxygenase** pathway might have been involved in the activation by PHSTD of the NADPH oxidase in PMNs.(ABSTRACT TRUNCATED AT 400 WORDS)

L10 ANSWER 14 OF 17 MEDLINE
ACCESSION NUMBER: 87064250 MEDLINE
DOCUMENT NUMBER: 87064250 PubMed ID: 3785138
TITLE: Purification, characterization, and structural properties of a single protein from rat basophilic leukemia (RBL-1) cells possessing 5-lipoxygenase and leukotriene A4 synthetase activities.
AUTHOR: Hogaboom G K; Cook M; Newton J F; Varrichio A; Shorr R G; Sarau H M; Crooke S T
SOURCE: MOLECULAR PHARMACOLOGY, (1986 Dec) 30 (6) 510-9. Journal code: NGR; 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198701
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19870115

AB Arachidonate 5-**lipoxygenase** of rat basophilic leukemia (RBL-1) cells was purified more than 1000-fold by gel filtration and anion exchange protein-high performance liquid chromatography (HPLC). Physical properties of the purified 5-**lipoxygenase** such as molecular **weight** (74,000-76,000), N-terminal sequence (30 amino acids), and amino acid composition were determined. The purified enzyme converted [14C]arachidonic acid at 20 degrees to [14C] 5-hydroperoxyeicosatetraenoic acid (5-HPETE) and to [14C]dihydroxyeicosatetraenoic acids (diHETEs). Utilizing [14C] 5(S)HPETE as substrate, the purified enzyme also converted the hydroperoxy acid to [14C]diHETES. The [14C]diHETE reaction products were identified primarily (greater than 80% of recovered radioactivity) as the nonenzymatic hydrolysis products of leukotriene A4 (i.e., 6-trans-leukotriene B4 and 12-epi-6-trans-leukotriene B4) by reverse phase HPLC, scanning spectrophotometry, and gas chromatography-mass spectrometry. The bioconversion of [14C] arachidonate and [14C]5(S)HPETE to reaction products by the purified enzyme was dependent on the presence of both Ca2+ and ATP. The enzymatic activities were **inhibited** in a similar manner by the **lipoxygenase inhibitors** **nordihydroguaiaretic acid**, diphenyldisulfide, and SK&F 86002. The data provide evidence that RBL-1 cell 5-**lipoxygenase** and leukotriene A4 synthetase activities reside on a single monomeric

protein with a free N-terminus and that they possess similar biochemical characteristics.

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L10 ANSWER 15 OF 17 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 86293219 MEDLINE
DOCUMENT NUMBER: 86293219 PubMed ID: 2426952
TITLE: Inhibition of bleomycin-induced pulmonary fibrosis by nordihydroguaiaretic acid. The role of alveolar macrophage activation and mediator production.
AUTHOR: Phan S H; Kunkel S L
CONTRACT NUMBER: HL-28737 (NHLBI)
HL-31237 (NHLBI)
HL-31963 (NHLBI)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1986 Aug) 124 (2) 343-52.
Journal code: 3RS; 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198609
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860917

AB The role of alveolar macrophage activation and release of mediators remains unclear. In this study, this role is examined with respect to the effects of relatively selective **inhibitors** of arachidonate metabolism on the pathogenesis of pulmonary fibrosis. CBA/J mice were administered bleomycin (0.037 units) endotracheally to induce pulmonary fibrosis. Daily intraperitoneal injections of a **lipoxygenase inhibitor**, **nordihydroguaiaretic acid** (**NDGA**) **inhibited** pulmonary fibrosis in a dose-dependent manner (15-25 mg/kg body **weight**), as assessed by both lung collagen synthesis and total lung hydroxyproline content. The less specific **inhibitor** BW755c was also effective at a dose of 25 mg/kg. In contrast, the cyclooxygenase **inhibitor**, ibuprofen (15 mg/kg), was completely ineffective. Correlated with this antifibrogenic activity of **NDGA** was the **inhibition** of several other parameters of bleomycin-induced pulmonary fibrosis. Bleomycin treatment caused a greater than threefold increase in the percentage of alveolar macrophages expressing Ia antigen (from 7.7% +/- 1.07% to 29.9% +/- 4.16% of total recoverable alveolar macrophages). **NDGA**, but not ibuprofen, **inhibited** this increase in a dose-dependent manner. Associated with this indication of macrophage stimulation was an increase in spontaneous macrophage production of fibroblast growth factor (MDGF) activity as a result of bleomycin instillation. This increase was also **inhibited** by **NDGA** treatment. In contrast, bleomycin treatment caused a **reduction** in alveolar macrophage interleukin-1 (IL-1) production, and **NDGA** treatment did not

alter this **reduction**, which suggests that MDGF is separate from IL-1 in this case, and that MDGF played a more dominant role, at least in this model of pulmonary fibrosis. This antifibrogenic activity of **NDGA** was accomplished without any **reduction** in spontaneous macrophage prostaglandin (PG)E2 production, which suggests the selectivity (versus cyclooxygenase pathway) of **NDGA** **inhibition** and the relative lack of importance of macrophage-derived PGE2 in modulating fibrogenesis in this model. The results of this study have thus demonstrated the importance of alveolar macrophage stimulation and increased production of MDGF in the pathogenesis of bleomycin-induced pulmonary fibrosis. The data also suggest that both macrophage parameters are subject to regulation by arachidonate metabolites.

AB . . . release of mediators remains unclear. In this study, this role is examined with respect to the effects of relatively selective **inhibitors** of arachidonate metabolism on the pathogenesis of pulmonary fibrosis. CBA/J mice were administered bleomycin (0.037 units) endotracheally to induce pulmonary fibrosis. Daily intraperitoneal injections of a **lipoxygenase inhibitor**, **nordihydroguaiaretic acid (NDGA)** **inhibited** pulmonary fibrosis in a dose-dependent manner (15-25 mg/kg body **weight**), as assessed by both lung collagen synthesis and total lung hydroxyproline content. The less specific **inhibitor** BW755c was also effective at a dose of 25 mg/kg. In contrast, the cyclooxygenase **inhibitor**, ibuprofen (15 mg/kg), was completely ineffective. Correlated with this antifibrogenic activity of **NDGA** was the **inhibition** of several other parameters of bleomycin-induced pulmonary fibrosis. Bleomycin treatment caused a greater than threefold increase in the percentage of alveolar macrophages expressing Ia antigen (from 7.7% +/- 1.07% to 29.9% +/- 4.16% of total recoverable alveolar macrophages). **NDGA**, but not ibuprofen, **inhibited** this increase in a dose-dependent manner. Associated with this indication of macrophage stimulation was an increase in spontaneous macrophage production of fibroblast growth factor (MDGF) activity as a result of bleomycin instillation. This increase was also **inhibited** by **NDGA** treatment. In contrast, bleomycin treatment caused a **reduction** in alveolar macrophage interleukin-1 (IL-1) production, and **NDGA** treatment did not alter this **reduction**, which suggests that MDGF is separate from IL-1 in this case, and that MDGF played a more dominant role, at least in this model of pulmonary fibrosis. This antifibrogenic activity of **NDGA** was accomplished without any **reduction** in spontaneous macrophage prostaglandin (PG)E2 production, which suggests the selectivity (versus cyclooxygenase pathway) of **NDGA** **inhibition** and the relative lack of importance of macrophage-derived PGE2 in modulating fibrogenesis in this model. The results of this study. . .

L10 ANSWER 16 OF 17 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 86287480 MEDLINE
DOCUMENT NUMBER: 86287480 PubMed ID: 3016755
TITLE: Lipoxygenase inhibitor and colchicine as anti-arthritic agents in the rat.
AUTHOR: Sabata S; Moshonov S; Zor U; Floman Y; Naor Z
SOURCE: PROSTAGLANDINS, LEUKOTRIENES AND MEDICINE, (1986 Jul) 23 (1) 95-102.
Journal code: P02; 8206868. ISSN: 0262-1746.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198609

ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860925

AB The non-steroidal anti-inflammatory agents do not have identical activities on the various pathways of arachidonic acid metabolism. The purpose of this study is to examine and compare the activities of colchicine, an anti-arthritic agent, indomethacin, a known prostaglandin synthesis **inhibitor** and **nordihydroguaiaretic acid (NDGA)**, a **lipoxygenase inhibitor**, in an experimental model of arthritis. Acute arthritis of the knee was induced in rats by injection of lipopolysaccharide (LPS) into the joints. Arthritis was characterized by an increase in joint diameter (18%), increased synovial **weight** (34%) and an increase in synovial prostaglandin E (PGE) production (56%). While administration of all of the agents examined abolished LPS-induced joint diameter and synovial **weight** increase, only indomethacin **reduced** increased PGE content. **NDGA** and colchicine had no **inhibitory** effect on LPS-induced PGE production, and moreover they actually stimulated PGE production when compared to control values. It is concluded that: Among the mediators of the inflammatory process are factors sensitive to colchicine and **NDGA** which are not PGs. **Lipoxygenase** products of arachidonic acid including leukotrienes may have an important role in inflammation. Leukotrienes and prostaglandins may act in concert in mediating the inflammatory process.

AB . . . of this study is to examine and compare the activities of colchicine, an anti-arthritic agent, indomethacin, a known prostaglandin synthesis **inhibitor** and **nordihydroguaiaretic acid (NDGA)**, a **lipoxygenase inhibitor**, in an experimental model of arthritis. Acute arthritis of the knee was induced in rats by injection of lipopolysaccharide (LPS) into the joints. Arthritis was characterized by an increase in joint diameter (18%), increased synovial **weight** (34%) and an increase in synovial prostaglandin E (PGE) production (56%). While administration of all of the agents examined abolished LPS-induced joint diameter and synovial **weight** increase, only indomethacin **reduced** increased PGE content. **NDGA** and colchicine had no **inhibitory** effect on LPS-induced PGE production, and moreover they actually stimulated PGE production when compared to control values. It is concluded that: Among the mediators of the inflammatory process are factors sensitive to colchicine and **NDGA** which are not PGs. **Lipoxygenase** products of arachidonic acid including leukotrienes may have an important role in inflammation. Leukotrienes and prostaglandins may act in concert. . .

L10 ANSWER 17 OF 17 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 86061432 MEDLINE
DOCUMENT NUMBER: 86061432 PubMed ID: 2415659
TITLE: Studies on the release of leukotrienes and histamine by human lung parenchymal and bronchial fragments upon immunologic and nonimmunologic stimulation. Effects of nordihydroguaiaretic acid, aspirin, and sodium cromoglycate.
AUTHOR: Salari H; Borgeat P; Fournier M; Hebert J; Pelletier G
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1985 Dec 1) 162 (6) 1904-15.
Journal code: I2V; 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 19900321

Last Updated on STN: 19970203
Entered Medline: 19860123

AB Fragments of human lung parenchyma or bronchi were studied by high performance liquid chromatography, gas chromatography-mass spectrometry, and bioassay for the biosynthesis of 5-**lipoxygenase** metabolites of arachidonic acid, and by radioenzymatic assay for the release of histamine, upon immunologic and nonimmunologic stimulation. Human lung parenchyma were passively sensitized with serum from timothy-positive allergic patients (radioallergosorbent test, 30-40%) and challenged with 0.5 microgram/ml of timothy allergen. Analysis of the incubation media showed the presence of LTB4, LTC4, LTD4, LTE4, and histamine. Maximum release of LTB4 and LTD4 was observed after 15 min of challenge (92.8 +/- 21, and 67.8 +/- 14 pmol/g tissue wet **weight**, respectively; mean +/- SEM) whereas maximum release of LTC4 was observed after 5 min of challenge (25 +/- 7.1 pmol). In parallel to leukotriene formation, histamine was released rapidly and reached a maximum after approximately 15 min of challenge (2.85 +/- 0.76 nmol/g tissue). When fragments of human lung parenchyma were stimulated with ionophore A23187 (4 microM), we observed a profile of leukotriene and histamine release similar to that seen in response to the allergen. Ionophore A23187 stimulated the release of two- to fivefold greater amounts of leukotrienes and histamine than did the allergen. Release of LTC4 and histamine was maximal after 5 min of stimulation (83 +/- 22.2 and 5.2 +/- 0.95 nmol/g tissue, respectively), whereas LTB4 and LTD4 release reached a maximum after 15 min (438 +/- 66.6 and 205 +/- 68 nmol/g tissue, respectively). In addition, human lung parenchyma metabolized LTB4 into omega-OH-LTB4 and omega-COOH-LTB4. This tissue also released 5-hydroxy-eicosatetraenoic acid (5-Hete), 12-Hete, and 15-Hete. Fragments of human lung bronchi also released a similar profile of leukotrienes (except LTC4) and histamine when challenged with the allergen or ionophore A23187. Maximum release of LTB4 and LTD4 by allergen or ionophore stimulation was observed after approximately 15 min (40 +/- 7.5 and 21 +/- 8 pmol/g tissue, respectively, upon allergen challenge; 100 +/- 13 and 47 +/- 10.6 pmol/g tissue, respectively, upon ionophore stimulation). The maximum release of histamine by bronchi was observed after approximately 15 min of allergen challenge and 5 min of ionophore stimulation (2.25 +/- 0.65 and 3.15 +/- 0.9 nmol/g tissue, respectively). The release of leukotrienes but not of histamine by human lung parenchyma upon both allergen and ionophore challenge was **inhibited** by **nordihydroguaiaretic acid** (**NDGA**) (ID50, 2 X 10(-6)M).(ABSTRACT TRUNCATED AT 400 WORDS)

AB . . . lung parenchyma or bronchi were studied by high performance liquid chromatography, gas chromatography-mass spectrometry, and bioassay for the biosynthesis of 5-**lipoxygenase** metabolites of arachidonic acid, and by radioenzymatic assay for the release of histamine, upon immunologic and nonimmunologic stimulation. Human lung. . . LTB4 and LTD4 was observed after 15 min of challenge (92.8 +/- 21, and 67.8 +/- 14 pmol/g tissue wet **weight**, respectively; mean +/- SEM) whereas maximum release of LTC4 was observed after 5 min of challenge (25 +/- 7.1 pmol).. . . respectively). The release of leukotrienes but not of histamine by human lung parenchyma upon both allergen and ionophore challenge was **inhibited** by **nordihydroguaiaretic acid** (**NDGA**) (ID50, 2 X 10(-6)M).(ABSTRACT TRUNCATED AT 400 WORDS)

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L10 ANSWER 6 OF 17 MEDLINE
ACCESSION NUMBER: 92255993 MEDLINE
DOCUMENT NUMBER: 92255993 PubMed ID: 1316134
TITLE: Platelet-activating factor provokes release of mucin-like glycoproteins from guinea pig respiratory epithelial cells

via a lipoxygenase-dependent mechanism.

AUTHOR: Adler K B; Akley N J; Glasgow W C
CORPORATE SOURCE: Department of Anatomy, College of Veterinary Medicine, North Carolina State University, Raleigh 27606.

CONTRACT NUMBER: HL-36736 (NHLBI)
HL-36982 (NHLBI)
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, (1992 May) 6 (5) 550-6.
Journal code: AOB; 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920626
Last Updated on STN: 19970203
Entered Medline: 19920616

AB Primary cultures of guinea pig tracheal epithelial cells maintained in an air/liquid interface system that maintains differentiated characteristics were grown to near confluence and exposed for 1 h to platelet-activating factor (PAF) on both apical and basal sides. PAF provoked release of high-molecular-**weight** mucin-like glycoproteins (MLG) from the cells, with maximal stimulation occurring at 10(-8) and 10(-9) M. The inactive form of PAF, lyso-PAF, was without effect. Indomethacin, the cyclooxygenase **inhibitor**, did not affect secretion stimulated by PAF, but nordihydroguiaretic acid (**NDGA**), a mixed cyclooxygenase and **lipoxygenase inhibitor**, attenuated secretion stimulated by PAF in a concentration-dependent manner. High performance liquid chromatography assay of the culture medium after addition of PAF revealed increased production of 15-, 12-, and 5-hydroxyeicosatetraenoic acids (15-, 12-, and 5-HETEs). The stimulatory effect of PAF on both mucin secretion and formation of HETEs was **inhibited** by the PAF receptor antagonists, CV-3988 and Ro 19 3704, with Ro 19 3704 acting at a concentration 10-fold lower than CV-3988 in **inhibiting** both effects. When added exogenously to the cell cultures, the combination of 5-, 12-, and 15-HETEs stimulated MLG release in a concentration-dependent manner. The results suggest that PAF stimulates release of MLG by guinea pig airway epithelium in vitro by a mechanism involving binding of PAF to receptors on epithelial cell surfaces, stimulation of **lipoxygenase** metabolism of arachidonic acid to HETEs within the epithelium, and stimulation of secretion by these epithelial-derived HETEs via an autocrine or paracrine mechanism.

AB . . . confluence and exposed for 1 h to platelet-activating factor (PAF) on both apical and basal sides. PAF provoked release of high-molecular-**weight** mucin-like glycoproteins (MLG) from the cells, with maximal stimulation occurring at 10(-8) and 10(-9) M. The inactive form of PAF, lyso-PAF, was without effect. Indomethacin, the cyclooxygenase **inhibitor**, did not affect secretion stimulated by PAF, but nordihydroguiaretic acid (**NDGA**), a mixed cyclooxygenase and **lipoxygenase inhibitor**, attenuated secretion stimulated by PAF in a concentration-dependent manner. High performance liquid chromatography assay of the culture medium after addition. . . 5-hydroxyeicosatetraenoic acids (15-, 12-, and 5-HETEs). The stimulatory effect of PAF on both mucin secretion and formation of HETEs was **inhibited** by the PAF receptor antagonists, CV-3988 and Ro 19 3704, with Ro 19 3704 acting at a concentration 10-fold lower than CV-3988 in **inhibiting** both effects. When added exogenously to the cell cultures, the combination of 5-, 12-, and 15-HETEs stimulated MLG release in. . . pig airway epithelium in vitro by a mechanism involving binding of PAF to receptors on epithelial cell surfaces, stimulation of **lipoxygenase** metabolism of arachidonic acid to HETEs within the epithelium, and stimulation of secretion by these epithelial-derived HETEs

via an autocrine. . .

L10 ANSWER 7 OF 17 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 92230850 MEDLINE
DOCUMENT NUMBER: 92230850 PubMed ID: 1566862
TITLE: Acetylcholine stimulates bronchial epithelial cells to release neutrophil and monocyte chemotactic activity.
AUTHOR: Koyama S; Rennard S I; Robbins R A
CORPORATE SOURCE: Research Service, Omaha Veterans Affairs Medical Center, Nebraska.
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1992 Apr) 262 (4 Pt 1) L466-71.
Journal code: 3U8; 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920607
Last Updated on STN: 19920607
Entered Medline: 19920521

AB Bronchial asthma is accompanied by inflammatory cell infiltration in the airway. Increased bronchial reactivity to cholinergic stimulation is well recognized in patients with bronchial asthma. Thus, we postulated that acetylcholine (ACh) stimulates bronchial epithelial cells (BEC) to release neutrophil and monocyte chemotactic activity (NCA and MCA). To test this hypothesis, bovine BEC monolayers were tested for NCA and MCA by a blind-well chemotactic chamber technique. BEC released NCA and MCA in response to ACh in a dose-dependent and time-dependent manner. Molecular sieve column chromatography revealed that ACh induced a single low-molecular-**weight** peak (near 400) for NCA and two low-molecular-**weight** peaks (near 12,000 and 400) for MCA. The release of NCA and MCA was **inhibited** by the **lipoxygenase inhibitors**, **nordihydroguaiaretic acid** and diethylcarbamazine. Cigarette smoke is a well-recognized stimulus for airway inflammation. To determine whether smoke might activate BEC to release NCA by stimulating nicotinic ACh receptors, we further characterized the ACh receptors, using nicotine and nicotinic and muscarinic receptor antagonists. Nicotine, the nicotinic receptor antagonist d-tubocurarine, and the M2 receptor antagonist gallamine did not modulate the release of NCA in response to ACh. In contrast, atropine and the M1 receptor antagonist, pirenzepine, **inhibited** the release of NCA. These data demonstrate that ACh stimulates BEC to release **lipoxygenase**-derived NCA and MCA through the muscarinic receptor.

AB . . . in response to ACh in a dose-dependent and time-dependent manner. Molecular sieve column chromatography revealed that ACh induced a single low-molecular-**weight** peak (near 400) for NCA and two low-molecular-**weight** peaks (near 12,000 and 400) for MCA. The release of NCA and MCA was **inhibited** by the **lipoxygenase inhibitors**, **nordihydroguaiaretic acid** and diethylcarbamazine. Cigarette smoke is a well-recognized stimulus for airway inflammation. To determine whether smoke might activate BEC to release. . . did not modulate the release of NCA in response to ACh. In contrast, atropine and the M1 receptor antagonist, pirenzepine, **inhibited** the release of NCA. These data demonstrate that ACh stimulates BEC to release **lipoxygenase**-derived NCA and MCA through the muscarinic receptor.

L10 ANSWER 8 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:171650 BIOSIS
DOCUMENT NUMBER: BA93:93975
TITLE: ENDOTHELIN-1-INDUCED TRITIUM INOSITOL PHOSPHATE

ACCUMULATION IN RAT TRACHEA.

AUTHOR(S): HENRY P J; RIGBY P J; SELF G J; PREUSS J M; GOLDIE R G
CORPORATE SOURCE: DEP. PHARMACOL., UNIV. WESTERN AUSTRALIA, NEDLANDS 6009, AUSTRALIA.

SOURCE: BR J PHARMACOL, (1992) 105 (1), 135-141.
CODEN: BJPCBM. ISSN: 0007-1188.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB 1 The effects of endothelin-1 (EF-1) and of the muscarinic cholinoceptor agonist, carbachol, on [3H]-inositol phosphate ([3H]-InsP) accumulation and smooth muscle contraction were determined in rat isolated tracheal tissue. 2 EF-1 (1 .mu.m) and carbachol (10 .mu.M) induced significant accumulation of [3H]-InsPs myo-[2-3H]-inositol-loaded rat tracheal segments. Several components of the tracheal wall including the airway smooth muscle band, the cartilaginous region and the intercartilaginous region generated significant levels of [3H]-InsPs in response to ET-1 and carbachol. Following stimulation with ET-1, a greater proportion of tracheal [3H]-InsPs were generated in the intercartilaginous region (49%) than in either the airway smooth muscle band (25%) or cartilagous region (26%). However, when the respective **weights** of these regions is taken into account, ET-1-induced accumulation of [3H]-InsPs was greatest in the airway smooth muscle band. The tracheal epithelium did not appear to generate [3H]-InsPs in response to ET-1 or modulate either basal or ET-1 induced accumulation of [3H]-InsPs in rat tracheal segments. 3 In the rat tracheal smooth muscle band, ET-1 caused a time- and concentration-dependent accumulation of [3H]-InsPs. Concentrations of ET-1 as low as 10 nM produced signficiant accumulation of [3H]-InsPs (1.25 .+-. 0.10 fold increase above basal levels of 295 .+-. 2 d.p.m. mg-1 wet wt., n = 3 experiments). At 10 .mu.M, the highest concentration used, ET-1 produced similar levels of [3H]-InsP accumulation (7.03 .+-. 0.55 fold above basal levels, n = 5) to that produced by a maximally effective concentration of carbachol (10 mM; 7.97 .+-. 0.31 fold increase above basal levels, n = 4). ET-1-induced accumulation of [3H]-InsPs was not significantly affected by indomethacin (5 .mu.M), **nordihydroguaiaretic acid** (**NDGA**, 10 .mu.M), WEB 2086 (10 .mu.M) or phosphoramidon (10 .mu.M). 4 ET-1 also produced concentration-dependent contractions of epithelium-denuded rat tracheal ring preparations. The mean concentration of ET-1 producing 50% of the maximum contractile response to carbachol (EC50) was 31 nM (95% confidence limits, 20-49 nM, n = 12). The presence of an intact tracheal epithelium, indomethacin (5 .mu.M), WEB 2086 (10 .mu.M) and phosphoramidon (10 .mu.M) had no significant effect on the mean EC50 for ET-1-induced contraction (n = 5). In contrast, **NDGA** (10 .mu.M) **inhibited** ET-1-induced contractions (4.0 fold increase in mean EC50, $P < 0.001$, n = 5). However, this effect of **NDGA** did not appear to be related to **inhibition** of leukotriene synthesis via **lipoxygenase** since the leukotriene antagonist SKF 104353 did not affect ET-1-induced contractions (n = 5) and moreover, leukotriene C4 and leukotriene D4 did not contract rat isolated tracheal smooth muscle preparations (n = 4). 5 The threshold concentrations of ET-1 that produced increases in smooth muscle contraction and [3H]-InsPs accumulation were similar, although the EC50 for [3H]-InsP accumulation was 2.9 fold greater than that for smooth muscle contraction. For carbachol, the EC50 for [3H]-InsP accumulation (mean EC50 = 5.0 .mu.M, 1.2-21 .mu.M, n = 4) was 25 fold greater than that for smooth muscle contraction (mean EC50 = 0.20 .mu.M, 0.17-0.24 .mu.M, n = 12). 6 It seems likely that ET-1 has a direct effect on InsP generation in rat tracheal smooth muscle and that this is largely responsible for the spasmogenic actions of this peptide.

AB. . . intercartilaginous region (49%) than in either the airway smooth muscle band (25%) or cartilagous region (26%). However, when the respective **weights** of these regions is taken into account, ET-1-induced accumulation of [3H]-InsPs was greatest in the airway smooth

muscle band. The. . . fold increase above basal levels, n = 4). ET-1-induced accumulation of [3H]-InsPs was not significantly affected by indomethacin (5 .mu.M), **nordihydroguaiaretic acid** (**NDGA**, 10 .mu.M), WEB 2086 (10 .mu.M) or phosphoramidon (10 .mu.M). 4 ET-1 also produced concentration-dependent contractions of epithelium-denuded rat tracheal. . . and phosphoramidon (10 .mu.M) had no significant effect on the mean EC50 for ET-1-induced contraction (n = 5). In contrast, **NDGA** (10 .mu.M) **inhibited** ET-1-induced contractions (4.0 fold increase in mean EC50, P < 0.001, n = 5). However, this effect of **NDGA** did not appear to be related to **inhibition** of leukotriene synthesis via **lipoxygenase** since the leukotriene antagonist SKF 104353 did not affect ET-1-induced contractions (n = 5) and moreover, leukotriene C4 and leukotriene. . .

L10 ANSWER 9 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 91358185 MEDLINE
DOCUMENT NUMBER: 91358185 PubMed ID: 1909312
TITLE: Cyclooxygenase pathway mediates lung injury induced by phorbol and platelets.
AUTHOR: Wang D; Chou C L; Hsu K; Chen H I
CORPORATE SOURCE: Department of Pharmacology, National Defense Medical Center, Taipei, Taiwan, Republic of China.
SOURCE: JOURNAL OF APPLIED PHYSIOLOGY, (1991 Jun) 70 (6) 2417-21. Journal code: HEG; 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911027
Last Updated on STN: 19911027
Entered Medline: 19911008

AB The role of platelets in lung injury has not been well defined. In the present study of isolated perfused rat lungs, phorbol myristate acetate (PMA; 0.15 microgram/ml) or platelets (6.7 X 10(4)/ml) alone did not discernibly change the pulmonary arterial pressure (PAP) or lung **weight** (LW). However, the combination of platelets and PMA drastically increased the PAP and LW (delta PAP 26.2 +/- 1.0 mmHg, delta LW 2.7 +/- 0.4 g). delta PAP was positively correlated with the increase in thromboxane B2 produced by infusion of platelets and PMA (thromboxane B2 = 35.6 + 0.97 delta PAP, r = 0.67, P less than 0.01). The hypertension and edema formation induced by PMA and platelets were strongly attenuated by indomethacin, an **inhibitor** of platelet cyclooxygenase (delta PAP 5.6 +/- 2.0 mmHg, P less than 0.001; delta LW 0.0 +/- 0.1 g, P less than 0.001), and by imidazole, an **inhibitor** of thromboxane A2 synthase (PAP 8.0 +/- 2.5 mmHg, P less than 0.001; LW 0.0 +/- 0.3 g, P less than 0.01). Inactivation of platelet **lipoxygenase** with **nordihydroguaiaretic acid** mildly depressed pulmonary pressure but did not affect delta LW (delta PAP 18.9 +/- 1.6 mmHg, P less than 0.05; delta LW 3.1 +/- 0.3 g, P greater than 0.05). In vitro experiments showed that the capacity of platelets to release oxygen radicals was only 2.6% of that found for granulocytes. These results suggest that platelets may be activated by PMA to increase PAP and vascular permeability.(ABSTRACT TRUNCATED AT 250 WORDS)

AB . . . (PMA; 0.15 microgram/ml) or platelets (6.7 X 10(4)/ml) alone did not discernibly change the pulmonary arterial pressure (PAP) or lung **weight** (LW). However, the combination of platelets and PMA drastically increased the PAP and LW (delta PAP 26.2 +/- 1.0 mmHg,. . . P less than 0.01). The hypertension and edema formation induced by PMA and platelets were strongly attenuated by indomethacin, an **inhibitor** of platelet cyclooxygenase (delta PAP 5.6 +/- 2.0 mmHg, P less than 0.001; delta LW 0.0 +/- 0.1 g, P less than 0.001), and by imidazole, an

inhibitor of thromboxane A2 synthase (PAP 8.0 +/- 2.5 mmHg, P less than 0.001; LW 0.0 +/- 0.3 g, P less than 0.01). Inactivation of platelet **lipoxygenase** with **nordihydroguaiaretic acid** mildly depressed pulmonary pressure but did not affect delta LW (delta PAP 18.9 +/- 1.6 mmHg, P less than 0.05;. . .

L10 ANSWER 10 OF 17 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 89341623 MEDLINE
DOCUMENT NUMBER: 89341623 PubMed ID: 2760546
TITLE: Identification of the major metabolite of 12-HETE produced by renal tubular epithelial cells.
AUTHOR: Gordon J A; Figard P H; Spector A A
CORPORATE SOURCE: Department of Internal Medicine, University of Iowa College of Medicine, Iowa City 52242.
CONTRACT NUMBER: HL-14230 (NHLBI)
SOURCE: JOURNAL OF LIPID RESEARCH, (1989 May) 30 (5) 731-8.
Journal code: IX3; 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198909
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19970203
Entered Medline: 19890915

AB The identification and polarity of release of the major metabolite of 12-HETE produced by cultured canine renal tubular epithelial cells was determined. When incubated with 1.0 microM [3H]12-HETE for 1 h, cultured Madin Darby Canine Kidney (MDCK) cells converted 35% of the radiolabeled 12-HETE to a more polar metabolite. Following high performance liquid chromatography isolation and chemical derivatization, gas-liquid chromatography combined with mass spectrometry was used to identify the compound as 8-hydroxyhexadecatrienoic acid [16:3(8-OH)]. The electron impact mass spectrum of the hydrogenated derivative contained major ions at m/z = 215 and 245, corresponding to cleavage on either side of the trimethylsilyl group, and chemical ionization with NH3 yielded a major ion at m/z = 359, corresponding to the protonated molecular **weight** of the methyl ester. Incubation with 25 mM alpha-naphthoflavone, 20 microM **nordihydroguaiaretic acid**, and 0.1 mM 4-pentenoic acid failed to **inhibit** the formation 16:3 (8-OH), suggesting that the formation of 16:3 (8-OH) is not mediated by the cytochrome P-450, **lipoxygenase**, or mitochondrial beta-oxidation pathways. When grown on fibronectin-treated polycarbonate filters, MDCK cells released the 16:3 (8-OH) in both the apical and basolateral directions, irrespective of which side the 12-HETE was encountered. These results demonstrate the conversion of 12-HETE to a 16-carbon monohydroxy derivative by renal tubular epithelium and suggest that this product can be released to either the potential urinary space or the kidney parenchyma and renal microcirculation.

AB . . . trimethylsilyl group, and chemical ionization with NH3 yielded a major ion at m/z = 359, corresponding to the protonated molecular **weight** of the methyl ester. Incubation with 25 mM alpha-naphthoflavone, 20 microM **nordihydroguaiaretic acid**, and 0.1 mM 4-pentenoic acid failed to **inhibit** the formation 16:3 (8-OH), suggesting that the formation of 16:3 (8-OH) is not mediated by the cytochrome P-450, **lipoxygenase**, or mitochondrial beta-oxidation pathways. When grown on fibronectin-treated polycarbonate filters, MDCK cells released the 16:3 (8-OH) in both the apical. . .

L10 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1988:88930 BIOSIS
DOCUMENT NUMBER: BA85:45702

TITLE: PURIFICATION AND PARTIAL CHARACTERIZATION OF RAT LIVER LIPOXYGENASE.
AUTHOR(S): MACIAS P; CARMEN PINTO M; CAMPILLO J E
CORPORATE SOURCE: DEP. DE BIOQUIMICA, FAC. DE CIENCIAS, UNIV. DE EXTREMADURA, E-06071 BADAJOZ, SPAIN.
SOURCE: Z NATURFORSCH B CHEM SCI, (1987) 42 (10), 1343-1348. CODEN: ZNBSEN.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB **Lipoxygenase** was purified from rat liver cytosolic fraction by a method involving two successive chromatographic steps on Sephacryl S-200 and Phenyl Spharose CL-4B. The enzyme has a molecular **weight** of 96 Kdal and it seems to be composed of two identical subunits. Chromatofocusing of the enzyme revealed a single band of activity at pI 6.3. The enzyme activity of the purified fraction showed maximum activity at pH 7.0 with a Km for linoleic acid of 1.4 .mu.M and is competitively **inhibited** by the specific **lipoxygenase inhibitor nordihydroguaiaretic acid**. The purified enzyme shows absorption and fluorescence spectra similar to those of **lipoxygenase** from other sources. However, the molecular **weight** of **lipoxygenase** purified from liver is found to be different from that of the enzyme from polymorphonuclear leukocytes. It is suggested that there are different isoenzymes of **lipoxygenases** in mammals.

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=> d ibib abs kwic 1-5

L10 ANSWER 1 OF 17 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001506649 MEDLINE
DOCUMENT NUMBER: 21438971 PubMed ID: 11554738
TITLE: trans-10,cis-12-Conjugated linoleic acid reduces leptin secretion from 3T3-L1 adipocytes.
AUTHOR: Kang K; Pariza M W
CORPORATE SOURCE: Food Research Institute, Department of Food Microbiology and Toxicology, University of Wisconsin-Madison, 1925 Willow Drive, Madison, Wisconsin 53706, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Sep 21) 287 (2) 377-82.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20011022
Entered Medline: 20011018

AB The trans10,cis12 (t10c12) isomer of conjugated linoleic acid (CLA) has been shown to **inhibit** heparin-releasable lipoprotein lipase activity, **reduce** lipid stores in cultured 3T3-L1 adipocytes, and, when fed to mice, **reduce** body fat gain. We now report that t10c12 CLA significantly **reduced** leptin secretion from cultured 3T3-L1 adipocytes, and **reduced** leptin mRNA levels within the cells. Similar effects were produced by conjugated nonadecadienoic acid (a 19-carbon CLA cognate that is more effective than CLA in **reducing** body fat gain in mice), the **lipoxygenase inhibitor nordihydroguaiaretic acid** (which is synergistic with CLA in **reducing** body fat gain in mice), and ciglitazone (TZD, a PPARgamma agonist). Feeding mice diet supplemented with 0.5% t10c12 CLA for 4 weeks significantly **reduced** body fat gain, serum leptin levels and adipocyte leptin mRNA expression, without affecting feed intake or body **weight**. These data provide new insights into apparent mechanistic similarities among t10c12 CLA, CNA, **NDGA**, and TZD. Copyright 2001 Academic Press.

AB The trans10,cis12 (t10c12) isomer of conjugated linoleic acid (CLA) has been shown to **inhibit** heparin-releasable lipoprotein lipase activity, **reduce** lipid stores in cultured 3T3-L1 adipocytes, and, when fed to mice, **reduce** body fat gain. We now report that t10c12 CLA significantly **reduced** leptin secretion from cultured 3T3-L1 adipocytes, and **reduced** leptin mRNA levels within the cells. Similar effects were produced by conjugated nonadecadienoic acid (a 19-carbon CLA cognate that is more effective than CLA in **reducing** body fat gain in mice), the **lipoxygenase inhibitor nordihydroguaiaretic acid** (which is synergistic with CLA in **reducing** body fat gain in mice), and ciglitazone (TZD, a PPARgamma agonist). Feeding mice diet supplemented with 0.5% t10c12 CLA for 4 weeks significantly **reduced** body fat gain, serum leptin levels and adipocyte leptin mRNA expression, without affecting feed intake or body **weight**. These data provide new insights into apparent mechanistic similarities among t10c12 CLA, CNA, **NDGA**, and TZD. Copyright 2001 Academic Press.

L10 ANSWER 2 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000127568 MEDLINE
DOCUMENT NUMBER: 20127568 PubMed ID: 10665802
TITLE: Bothrops lanceolatus (Fer de lance) venom induces oedema formation and increases vascular permeability in the mouse hind paw.
AUTHOR: de Araujo A L; de Souza A O; da Cruz-Hofling M A; Flores C A; Bon C
CORPORATE SOURCE: Departamento de Farmacologia, Faculdade de Ciencias Medices, Universidade Estadual de Campinas, SP, Brazil.
SOURCE: TOXICON, (2000 Feb) 38 (2) 209-21.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000217

AB The ability of snake venoms to increase vascular permeability and to induce oedema through the release of pharmacologically active substances is well known. We have studied the oedema and vascular permeability induced by Bothrops lanceolatus venom in male Swiss white mice. Paw oedema was induced by the subplantar injection of B. lanceolatus venom (125-1000 ng/paw) and was quantified as the increase in paw **weight**. Changes in vascular permeability were assessed by measuring the amount of

Evans blue dye extravasation. The oedema and the increase in vascular permeability were maximal within 2 h and had resolved after 24 h. The administration of the vasodilator iloprost (20 ng/paw) immediately after B. lanceolatus venom potentiated the oedema and the increase in vascular permeability by approximately four-fold. Pretreating the mice with indomethacin, dexamethasone, **NDGA** or BW A4C **inhibited** the venom-induced oedema and the increase in vascular permeability. In contrast, histamine, serotonin and PAF-acether antagonists (mepyramine, cyproheptadine and WEB 2086, respectively) were ineffective. Histological examination showed that B. lanceolatus venom (250 ng and 500 ng/paw) caused thickening of the inner dermal layers which was accompanied by extensive intercellular spaces indicative of oedema. In addition, there was a marked infiltration of inflammatory cells, particularly neutrophils, into the underlying muscle layer. The latter, however, remained morphologically unaffected during the 3 h of observation. Venom doses larger than 500 ng/paw produced intense haemorrhage. These results indicate that B. lanceolatus venom induces oedema and increases vascular permeability in the mouse hind paw. The principal mediators of this inflammatory response are cyclooxygenase and **lipoxygenase** products.

AB . . . was induced by the subplantar injection of B. lanceolatus venom (125-1000 ng/paw) and was quantified as the increase in paw **weight** . Changes in vascular permeability were assessed by measuring the amount of Evans blue dye extravasation. The oedema and the increase. . . lanceolatus venom potentiated the oedema and the increase in vascular permeability by approximately four-fold. Pretreating the mice with indomethacin, dexamethasone, **NDGA** or BW A4C **inhibited** the venom-induced oedema and the increase in vascular permeability. In contrast, histamine, serotonin and PAF-acether antagonists (mepyramine, cyproheptadine and WEB. . . oedema and increases vascular permeability in the mouse hind paw. The principal mediators of this inflammatory response are cyclooxygenase and **lipoxygenase** products.

L10 ANSWER 3 OF 17 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96005829 MEDLINE
DOCUMENT NUMBER: 96005829 PubMed ID: 7558126
TITLE: Immunoregulatory activities of eicosanoids in the rainbow trout (Oncorhynchus mykiss).
AUTHOR: Knight J; Rowley A F
CORPORATE SOURCE: School of Biological Sciences, University of Wales, Swansea.
SOURCE: IMMUNOLOGY, (1995 Jul) 85 (3) 389-93.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19970203
Entered Medline: 19951106

AB Eicosanoids such as prostaglandins (PG), leukotrienes (LT) and lipoxins (LX) have been shown to be potent immunoregulatory molecules in mammals. To determine if they have similar roles in 'lower' animals, rainbow trout (Oncorhynchus mykiss) were immunized with either sheep erythrocytes or Aeromonas salmonicida in the presence or absence of the stable analogue of PGE2, 16,16-dimethyl-PGE2, and the number of plaque-forming cells (PFC) or specific antibody levels determined. The higher dose of 16,16-dimethyl-PGE2 (200 micrograms/kg body **weight**) caused a significant **reduction** in both PFC number and antibody titre compared with the control. The effect of PGE2, PGE3, 16,16-dimethyl-PGE2, LTB4, LTB5, LXA4, 12-HETE and 12-HEPE on PFC generation following the in

vitro challenge of trout splenocytes with sheep erythrocytes was also determined. All of the prostaglandins tested showed a dose-dependent **inhibition** of PFC after 11 days in culture, while of the remaining eicosanoids only LXA4 had any effect on PFC number, with a dose-dependent stimulatory effect. The cyclo-oxygenase **inhibitor**, indomethacin, also caused a stimulation in the number of PFC generated, with a maximal effect at c. 25 microM, while the lipooxygenase **inhibitors**, esculetin and **nordihydroguaiaretic acid** (5-100 microM), had no significant effect on PFC generation at all concentrations tested. The present results show that, as in mammals, prostaglandins and the cyclo-oxygenase pathway are also important in the regulation of the piscine humoral immune response. Of the **lipoxygenase** products tested, however, only LXA4 had any significant effect on PFC generation, suggesting that these compounds have only a limited role to play in immune regulation in this organism. Overall this work shows that eicosanoids have a long evolutionary history in immunoregulation, probably dating back at least to the appearance of bony fish some 400 million years ago.

AB . . . and the number of plaque-forming cells (PFC) or specific antibody levels determined. The higher dose of 16,16-dimethyl-PGE2 (200 micrograms/kg body **weight**) caused a significant **reduction** in both PFC number and antibody titre compared with the control. The effect of PGE2, PGE3, 16,16-dimethyl-PGE2, LTB4, LTB5, LXA4,. . . in vitro challenge of trout splenocytes with sheep erythrocytes was also determined. All of the prostaglandins tested showed a dose-dependent **inhibition** of PFC after 11 days in culture, while of the remaining eicosanoids only LXA4 had any effect on PFC number, with a dose-dependent stimulatory effect. The cyclo-oxygenase **inhibitor**, indomethacin, also caused a stimulation in the number of PFC generated, with a maximal effect at c. 25 microM, while the lipooxygenase **inhibitors**, esculetin and **nordihydroguaiaretic acid** (5-100 microM), had no significant effect on PFC generation at all concentrations tested. The present results show that, as in. . . mammals, prostaglandins and the cyclo-oxygenase pathway are also important in the regulation of the piscine humoral immune response. Of the **lipoxygenase** products tested, however, only LXA4 had any significant effect on PFC generation, suggesting that these compounds have only a limited. . .

L10 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:505229 BIOSIS
DOCUMENT NUMBER: PREV199497518229
TITLE: Lipoxygenase is an abundant protein in cucumber exudates.
AUTHOR(S): Avdiushko, Sergei A.; Ye, Xiang S.; Kuc, Joseph; Hildebrand, David F. (1)
CORPORATE SOURCE: (1) Dep. Agronomy, Univ. Kentucky, Lexington, KY 40546 USA
SOURCE: Planta (Heidelberg), (1994) Vol. 193, No. 3, pp. 349-357. ISSN: 0032-0935.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The presence of **lipoxygenase** (LOX) has been reported in many plant organs. High LOX activity (1-2 mu-katal/mg protein) was detected in exudates from cut cucumber (Cucumis sativus L.) stems and petioles. Exudate LOX had a pH optimum of 5.0, an estimated molecular **weight** of 95 kDa and cross-reacted on sodium-dodecyl-sulfate gels with anti-LOX antibodies raised against soybean leaf LOX isoenzymes. **Lipoxygenase** activity was detected on native gels stained with o-dianisidine using linoleic acid as a substrate. Enzyme activity was similar with linoleic and linolenic acid and 2 times greater with arachidonic acid as substrate. At pH 6.8, LOX metabolized linoleic acid into 13- and 9-hydroperoxides at a ratio of 1:2. Linolenic acid was preferentially oxidized at carbon 13. **Lipoxygenase** activity was **inhibited** by n-propyl gallate (IC-50 300 nM) and

nordihydroguaiaretic acid (IC-50 25 nM), but not by nonsteroidal anti-inflammatory drugs. LOX activity was enhanced 4.5-fold by 300 mM Ca-2+. Spermine at 1 mM, and putrescine and spermidine at 2 mM completely **inhibited** LOX activity, but at low concentrations spermine (100 mM) and spermidine (100-500 mM) significantly stimulated LOX activity: 8- and 4.5-fold, respectively. Tissue printing of stem, petiole and hypocotyl sections with subsequent incubation with the antiserum raised against soybean leaf LOX revealed the presence of LOX in the internal and external phloem and in the sieve tubes.

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L10 ANSWER 5 OF 17 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 93231391 MEDLINE
DOCUMENT NUMBER: 93231391 PubMed ID: 8386112
TITLE: Arachidonic acid-induced insulin secretion from rat islets of Langerhans is not mediated by protein phosphorylation.
AUTHOR: Basudev H; Jones P M; Persaud S J; Howell S L
CORPORATE SOURCE: Biomedical Sciences Division, King's College London, UK.
SOURCE: MOLECULAR AND CELLULAR ENDOCRINOLOGY, (1993 Feb) 91 (1-2) 193-9.
Journal code: E69; 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930604
Last Updated on STN: 19970203
Entered Medline: 19930520

AB Arachidonic acid (AA) stimulated protein phosphorylation in electrically permeabilised islets, most notably of an islet protein of approximate molecular **weight** 18 kDa. This protein did not appear to be a substrate for cAMP-dependent protein kinase. The AA-induced protein phosphorylation was mediated by unmetabolised AA since the **lipoxygenase inhibitor**, nordihydroguaretic acid (**NDGA**), or the cyclooxygenase **inhibitor**, indomethacin, did not significantly **reduce** AA-induced phosphorylation. Although saturated fatty acids did not stimulate phosphorylation of islet proteins, a number of cis-unsaturated fatty acids, other than AA, induced 32P incorporation into an 18 kDa protein. However, some fatty acids which stimulated protein phosphorylation had no effect on insulin secretion in experiments where AA clearly stimulated insulin secretion. AA stimulated protein kinase C (PKC) activity extracted from islets but several fatty acids which induced protein phosphorylation had no significant effect on PKC activity in vitro. 50 nM staurosporine had no effect on AA-induced

protein phosphorylation but this concentration of staurosporine markedly **inhibited** PKC activity. 200 nM staurosporine caused complete **inhibition** of the AA-induced phosphorylation without having any effect on AA-induced insulin secretion. These results suggest that AA and some other fatty acids can promote 32P incorporation into islet proteins, independently of PKC activation, and that AA-induced phosphorylation is not required for insulin secretory responses to AA.

AB Arachidonic acid (AA) stimulated protein phosphorylation in electrically permeabilised islets, most notably of an islet protein of approximate molecular **weight** 18 kDa. This protein did not appear to be a substrate for cAMP-dependent protein kinase. The AA-induced protein phosphorylation was mediated by unmetabolised AA since the **lipoxygenase inhibitor**, nordihydroguaretic acid (**NDGA**), or the cyclooxygenase **inhibitor**, indomethacin, did not significantly **reduce** AA-induced phosphorylation. Although saturated fatty acids did not stimulate phosphorylation of islet proteins, a number of cis-unsaturated fatty acids, other. . . PKC activity in vitro. 50 nM staurosporine had no effect on AA-induced protein phosphorylation but this concentration of staurosporine markedly **inhibited** PKC activity. 200 nM staurosporine caused complete **inhibition** of the AA-induced phosphorylation without having any effect on AA-induced insulin secretion. These results suggest that AA and some other. . .

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   4 FILES SEARCHED...
L2         7648 (".BETA.,.GAMMA.-DIMETHYL-.ALPHA.,.DELTA.-BIS(3,4-DIHYDROXYPHENY
                L)BUTANE"/BI OR "BUTANE, 1,4-BIS(3,4-DIHYDROXYPHENYL)-2,3-DIMETH
                YL-"/BI OR "DIHYDRONORGUAIARETIC ACID"/BI OR "DINORGUAIARETIC
                ACID, DIHYDRO-"/BI OR NDGA/BI OR "NORDIHYDROGUAIARETIC ACID"/BI
                OR "NORGUAIARETIC ACID, DIHYDRO-"/BI OR "1,4-BIS(3,4-DIHYDROXYPH
                ENYL)-2,3-DIMETHYLBUTANE"/BI OR "4,4'-(2,3-DIMETHYL-1,4-BUTANEDI
                YL)BIS(PYROCATECHOL)"/BI OR "4,4'-(2,3-DIMETHYLTETRAMETHYLENE)DI
                PYROCATECHOL"/BI OR 500-38-9/BI)

=> s lipid? or fat
L3      1163991 LIPID? OR FAT

=> s l2 and l3
L4         1101 L2 AND L3

=> s l2 (s) l3
L5          481 L2 (S) L3

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6          346 DUP REM L5 (135 DUPLICATES REMOVED)

=> log h
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      12.42      13.36

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:49:39 ON 16 MAY 2002


Welcome to STN International!  Enter x:x

LOGINID:ssspta1617srh

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, HCAPLUS, IPA, BIOSIS, USPATFULL'
AT 18:37:04 ON 16 MAY 2002
FILE 'MEDLINE' ENTERED AT 18:37:04 ON 16 MAY 2002
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FILE 'HCAPLUS' ENTERED AT 18:37:04 ON 16 MAY 2002
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'IPA' ENTERED AT 18:37:04 ON 16 MAY 2002
COPYRIGHT (C) 2002 American Society of Hospital Pharmacists (ASHP)
FILE 'BIOSIS' ENTERED AT 18:37:04 ON 16 MAY 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)
FILE 'USPATFULL' ENTERED AT 18:37:04 ON 16 MAY 2002
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      12.42      13.36

=> d his

     (FILE 'HOME' ENTERED AT 17:42:44 ON 16 MAY 2002)

     FILE 'REGISTRY' ENTERED AT 17:42:51 ON 16 MAY 2002
L1             1 S 500-38-9
                 SEL RN NAME L1

     FILE 'MEDLINE, HCAPLUS, IPA, BIOSIS, USPATFULL' ENTERED AT 17:43:19 ON 16
     MAY 2002
L2          7648 S E1-11
L3       1163991 S LIPID? OR FAT
L4          1101 S L2 AND L3
L5           481 S L2 (S) L3
L6           346 DUP REM L5 (135 DUPLICATES REMOVED)

=> s treat? or therap?
   4 FILES SEARCHED...
L7       8894567 TREAT? OR THERAP?

=> s l7 (s) l6
L8            46 L7 (S) L6

=> d ibib abs kwic 43-46

L8   ANSWER 43 OF 46  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:    1982:252093  BIOSIS
DOCUMENT NUMBER:     BA74:24573
TITLE:               ENDO TOXIN LIPO POLY SACCHARIDE STIMULATES IN-VITRO
                     MIGRATION OF MACROPHAGES FROM LIPO POLY SACCHARIDE
                     RESISTANT MICE BUT NOT FROM LIPO POLY SACCHARIDE SENSITIVE
                     MICE.
AUTHOR(S):           VERGHESE M W; SYNDERMAN R
CORPORATE SOURCE:    BOX 3982, DUKE UNIV. MED. CENT., DURHAM, N.C. 27710.
SOURCE:              J IMMUNOL, (1982) 128 (2), 608-613.
                     CODEN: JOIMA3. ISSN: 0022-1767.
FILE SEGMENT:        BA; OLD
LANGUAGE:            English
AB   Lipopolysaccharide (LPS) induces strikingly different inflammatory
     responses in LPS-resistant and -susceptible mice. The effects of LPS on
     the in vitro migration of macrophages and polymorphonuclear leukocytes
     from such animals were studied. LPS, in the absence of serum, stimulated
     the chemokinetic migration of elicited macrophages from the LPS-resistant
     C3H/HeJ and C57BL10/ScCR mice; migration of macrophages from the
     susceptible C3H/HeN and C57BL10/SN mice was either unaffected or slightly
     depressed by LPS. Doses of LPS as low as 50 ng/ml induced chemokinesis of
     C3H/HeJ macrophages. The strain differences between resistant and
     susceptible mice were observed with several different LPS preparations.
     Macrophage chemotaxis towards zymosan- or LPS-activated mouse serum was
```

similar in resistant and susceptible strains. Deproteinized LPS and **lipid** A preparations also induced migration of C3H/HeJ macrophages; **treatment** of LPS with polymyxin B abolished its stimulatory effects. Macrophages from C3H/HeJ mice must therefore respond to the **lipid** A moiety of LPS. No evidence was found that the strain characteristic migratory responses to LPS were influenced by differential stimulation of arachidonic acid metabolism by LPS in the cells: indomethacin, an inhibitor of prostaglandin synthesis, did not alter migration to either LPS- or zymosan-activated mouse serum in macrophages from resistant or susceptible mice; **nordihydroguaiaretic acid** and eicosatetraynoic acid, inhibitors of the production of potentially chemotactic hydroxyeicosatetraenoic acid, reduced migration toward both LPS- and zymosan-activated mouse serum by C3H/HeJ macrophages and toward zymosan-activated mouse serum by C3H/HeN macrophages. Strain differences in migratory responses to LPS were restricted to macrophages in that polymorphonuclear leukocytes of both strains failed to respond to LPS. These in vitro findings correlate with some of the in vivo inflammatory responses to LPS in resistant and susceptible mice.

AB. . . LPS preparations. Macrophage chemotaxis towards zymosan- or LPS-activated mouse serum was similar in resistant and susceptible strains. Deproteinized LPS and **lipid** A preparations also induced migration of C3H/HeJ macrophages; **treatment** of LPS with polymyxin B abolished its stimulatory effects. Macrophages from C3H/HeJ mice must therefore respond to the **lipid** A moiety of LPS. No evidence was found that the strain characteristic migratory responses to LPS were influenced by differential. . . prostaglandin synthesis, did not alter migration to either LPS- or zymosan-activated mouse serum in macrophages from resistant or susceptible mice; **nordihydroguaiaretic acid** and eicosatetraynoic acid, inhibitors of the production of potentially chemotactic hydroxyeicosatetraenoic acid, reduced migration toward both LPS- and zymosan-activated mouse. . .

L8 ANSWER 44 OF 46 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1978:204611 BIOSIS
DOCUMENT NUMBER: BA66:17108
TITLE: AGING OF NEUROSPORA-CRASSA PART 5 LIPID PER OXIDATION AND DECAY OF RESPIRATORY ENZYMES IN AN INOSITOL AUXOTROPH.
AUTHOR(S): RANA R S; MUNKRES K D
CORPORATE SOURCE: LAB. GENET., UNIV. WIS., MADISON, WIS. 53706, USA.
SOURCE: MECH AGEING DEV, (1978) 7 (4), 241-272.
CODEN: MAGDA3. ISSN: 0047-6374.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB An inositol auxotroph of N. crassa was grown in liquid culture with various inositol concentrations. Although the initial exponential growth rate was independent of the initial inositol concentration and equivalent to that of wild type, growth ceased prematurely with limiting concentrations. The period from the time of premature decline of growth rate until the time when cells begin to die at an exponential rate is defined as the senescence period. Comparisons of age-dependent changes in clones cultured with optimal and limiting inositol revealed that the latter accumulate more fluorescent pigment (lipofuscin) and that their mitochondria contained excessive concentrations of malondialdehyde, exhibited excessive rates of non-enzymatic **lipid** peroxidation in vitro and an age-dependent decline of specific activities of respiratory enzymes of the inner membrane. Cellular respiratory capacity was abnormal at an early age and deteriorated with increasing age. The in vitro rate of non-enzymatic **lipid** peroxidation was inversely correlated with the activities of the enzymes at various culture ages. Most of these abnormalities were evident in 9 h old clones prior to the onset of

senescence, becoming more severe during senescence. Culture with either **nordihydroguaiaretic acid** or hydrocortisone completely or partly prevented the occurrence of the biochemical abnormalities. Since these drugs also alleviate deterioration of clonal growth rates and cellular death, the observation that they protect mitochondria from the development of symptoms related to abnormal membranes and **lipid** peroxidation offers additional support to the hypothesis that their action is that of antioxidant and membrane stabilizer, respectively, and therefore, provides a molecular basis for their **therapeutic** role in vivo.

AB. . . latter accumulate more fluorescent pigment (lipofuscin) and that their mitochondria contained excessive concentrations of malondialdehyde, exhibited excessive rates of non-enzymatic **lipid** peroxidation in vitro and an age-dependent decline of specific activities of respiratory enzymes of the inner membrane. Cellular respiratory capacity was abnormal at an early age and deteriorated with increasing age. The in vitro rate of non-enzymatic **lipid** peroxidation was inversely correlated with the activities of the enzymes at various culture ages. Most of these abnormalities were evident in 9 h old clones prior to the onset of senescence, becoming more severe during senescence. Culture with either **nordihydroguaiaretic acid** or hydrocortisone completely or partly prevented the occurrence of the biochemical abnormalities. Since these drugs also alleviate deterioration of clonal. . . rates and cellular death, the observation that they protect mitochondria from the development of symptoms related to abnormal membranes and **lipid** peroxidation offers additional support to the hypothesis that their action is that of antioxidant and membrane stabilizer, respectively, and therefore, provides a molecular basis for their **therapeutic** role in vivo.

L8 ANSWER 45 OF 46 USPATFULL

ACCESSION NUMBER:	1999:7255 USPATFULL
TITLE:	Method for induction of tumor cell apoptosis with chemical inhibitors targeted to 12-lipoxygenase
INVENTOR(S):	Tang, Dean G., Troy, MI, United States Honn, Kenneth V., Grosse Pointe Woods, MI, United States
PATENT ASSIGNEE(S):	Biomide Investment Limited Partnership, Grosse Pointe Farms, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5861268		19990119
APPLICATION INFO.:	US 1996-652369		19960523 (8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Hollinden, Gary E.
ASSISTANT EXAMINER:	Jones, Dameron
LEGAL REPRESENTATIVE:	McLeod, Ian C.
NUMBER OF CLAIMS:	34
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	41 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT:	1312

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and test kit for determining tumor cell apoptosis by inhibition of 12-lipoxygenase is described. A method for selectively inducing tumor cell apoptosis by inhibiting 12-lipoxygenase is also described. The preferred compounds are selected from the group consisting of a cyclic hydroxamic acid; and an aryl aliphatic acid; nordihydro guaiaretic acid (NDGA) and N-benzyl-N-hydroxy-5-phenylpentanamide (BHPP).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . cells. Inhibition/blocking of 12-LOX activity with either general or selective inhibitors will trigger the apoptotic cell death. To determine whether **NDGA**-induced apoptosis is unique to W256 cells, the effect of **NDGA** was screened on several cultured normal and tumor cells derived from human, rat, and mouse. As shown in FIG. 3A, **NDGA** also induced apoptosis of some tumor cells other than W256 cells. MTLn-3, a rat mammary adenocarcinoma cell line which expressed 12-LOX (FIG. 3A, left panel), showed high spontaneous apoptosis, which was further enhanced by **NDGA** as well as by 12-LOX-selective inhibitors BHPP, and, much less dramatically, CDC and baicalein (FIG. 3A, right panel). COX inhibitor,. . . 5-LOX (Balcarek, J. M., et al., J. Biol. Chem. 263:13937-13941 (1988)). Whether they also express 12- and/or 15-LOX is unknown. **Treatment** of REL-1 cells with **NDGA** at .gtoreq.25 .mu.M of **NDGA** induced apoptosis (FIG. 3B). On the other hand, **treatment** of cells with 5-LOX inhibitors AA-861, caffeic acid, or 5,6-dehydro-arachidonic acid at up to 100 .mu.M did not induce apoptotic cell death (data not shown), suggesting that **NDGA** -induced RBL-1 apoptosis may be mediated by its effects on 12- and/or 15-LOX but not 5-LOX. HEL (human erythroleukemia) cells express. . . D., et al., Proc. Natl. Acad. Sci., USA 87:5638-5642 (1990)) and, most probably, also express other LOXs. At .gtoreq.25 .mu.M, **NDGA** also induced apoptosis of HEL cells (FIGS. 3C-3E). In contrast, **NDGA**, BHPP or a 12-LOX-specific antisense oligonucleotide (5'-CTCAGGAGGGTGTAAACA-3'--SEQ ID NO:6) did not induce apoptosis of rat aortic endothelial cells (RAEC) although. . . mouse pulmonary capillary (Tang, D. G., et al., Int. J. Cancer 60:418-425 (1995d)) endothelial cells also did not respond to **NDGA** (data not shown) although it is known that endothelial cells possess various LOX activities (Spector, A. A., et al., Prog. **Lipid** Res. 27:271-323 (1988); Rosolowsky, M., and W. B. Campbell, Biochem. Biophys. Acta 1299:267-277 (1996)).

L8 ANSWER 46 OF 46 USPATFULL

ACCESSION NUMBER:	85:73696 USPATFULL
TITLE:	Meat curing compositions and method of use
INVENTOR(S):	Rubin, Leon J., Toronto, Canada Diosady, Levente L., Toronto, Canada Shahidi, Fereidoon, Toronto, Canada Wood, Darrell F., Nepean, Canada
PATENT ASSIGNEE(S):	Canadian Patents and Development Limited, Ottawa, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4559234		19851217	
APPLICATION INFO.:	US 1984-615117		19840530	(6)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Corbin, Arthur L.
LEGAL REPRESENTATIVE:	Thomson, Alan A.
NUMBER OF CLAIMS:	16
EXEMPLARY CLAIM:	1
LINE COUNT:	800

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions for curing meats comprising dinitrosyl ferrohemochrome and at least one antioxidant, at least one sequestering agent and at least one antimicrobial agent. Such compositions bestow similar color, flavor, and microbiological stability as that associated with nitrite-treated meats.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD **Nordihydroguaiaretic acid** (**NDGA**), which is most effective in preventing the oxidation of phospholipids, was approved by the Meat Inspection Branch of the U.S.. . . in 1943, and was later patented (W. M. Lauer, U.S. Pat. No. 2,373,192) for use in lard and rendered pork **fat**. Our results indicate a slight darkening of the meat systems **treated** with this reagent. Although no organoleptic tests were carried out, it is known that the reagent has a slightly bitter taste. Catechol, which may be considered as the parent compound for **NDGA**, is a slightly better antioxidant than its derivative **NDGA**. Dipping bacon pieces in **fat** solutions of **NDGA** and BHA has been found to increase the stability of the product and the use of aqueous solutions or suspensions of **NDGA**, PG or BHA with or without synergists, were patented by S. L. Komarick and L. H. Hall, U.S. Pat. No.. . .

=> d ibib abs kwic 40-42

L8 ANSWER 40 OF 46 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:22568 BIOSIS
DOCUMENT NUMBER: PREV200200022568
TITLE: Lipoxygenase and cytochrome P450 pathway are associated with arachidonic acid-induced neuronal death in mixed cortical neurons.
AUTHOR(S): Kwon, K. J. (1); Kim, E. J. (1); Park, J. Y. (1); Lee, S. H. (1); Moon, C. H. (1); Baik, E. J. (1)
CORPORATE SOURCE: (1) Dept of Physio, Sch of Med, Ajou Univ, Suwon South Korea
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2323. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Arachidonic acid (AA) is a component of membrane **lipids** that has been implicated as a messenger both in physiological and pathological processes. AA release from cellular membranes due to trauma, and ischemic injury may be one of the principal destructive events that can lead to progressive injury. AA serves as a precursor to a number of biologically active **lipids** such as prostaglandins, thromboxane, and leukotrienes. In this study, we investigate the roles of lipoxygenase and cytochrome P450 in AA-induced neuronal toxicity, mixed cortical neurons in culture were exposed to AA under chemically-defined conditions. AA showed a significant toxicity to mixed cortical neurons in a dose dependent manner, when assessed by LDH release, MTT assay, and propidium iodide uptake. AA **treatment** increased oxidative stress and decreased cell viability. The AA neurotoxicity was attenuated by cytochrome P450 inhibitors, SKF525A and metyrapone. Similarly to cytochrome P450 inhibitors, pan-lipoxygenase inhibitor **NDGA** mitigated AA-induced neurotoxicity. And also AA861 and baicalein, selective inhibitors for 5- and 12-lipoxygenase respectively, showed a significant cytoprotective effect. AA **treatment** increased oxidative stress and this increase in intracellular level of ROS was reduced by cytochrome P450 inhibitors and lipoxygenase inhibitors in mixed cortical neuron. AA depleted the GSH level, which was reversed by cytochrome P450 inhibitors and lipoxygenase inhibitors. Our data indicate that AA-induced neurotoxicity is mediated by at least in part free radical production, in which cytochrome P450 and lipoxygenase pathway are involved.
AB Arachidonic acid (AA) is a component of membrane **lipids** that has been implicated as a messenger both in physiological and pathological

processes. AA release from cellular membranes due to. . . principal destructive events that can lead to progressive injury. AA serves as a precursor to a number of biologically active **lipids** such as prostaglandins, thromboxane, and leukotrienes. In this study, we investigate the roles of lipoxygenase and cytochrome P450 in AA-induced. . . mixed cortical neurons in a dose dependent manner, when assessed by LDH release, MTT assay, and propidium iodide uptake. AA **treatment** increased oxidative stress and decreased cell viability. The AA neurotoxicity was attenuated by cytochrome P450 inhibitors, SKF525A and metyrapone. Similarly to cytochrome P450 inhibitors, pan-lipoxygenase inhibitor **NDGA** mitigated AA-induced neurotoxicity. And also AA861 and baicalein, selective inhibitors for 5- and 12-lipoxygenase respectively, showed a significant cytoprotective effect. AA **treatment** increased oxidative stress and this increase in intracellular level of ROS was reduced by cytochrome P450 inhibitors and lipoxygenase inhibitors. . .

L8 ANSWER 41 OF 46 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:235847 BIOSIS
DOCUMENT NUMBER: PREV199800235847
TITLE: Cyanide-induced generation of oxidative species: Involvement of nitric oxide synthase and cyclooxygenase-2.
AUTHOR(S): Gunasekar, P. G.; Borowitz, J. L.; Isom, Gary E. (1)
CORPORATE SOURCE: (1) Neurotoxicol. Lab., Dep. Med. Chem. Mol. Pharmacol., Purdue Univ., West Lafayette, IN 47907-1334 USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (April, 1998) Vol. 285, No. 1, pp. 236-241. ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In cerebellar granule cells, potassium cyanide (KCN) activates the NMDA receptor resulting in generation of nitric oxide and reactive oxygen species (ROS). To study the mechanism by which KCN stimulates ROS generation, the action of cyanide on the enzymatic pathways known to generate ROS were studied. The oxidant-sensitive fluorescent dye, 2,7-dichlorofluorescin was used to measure intracellular levels of nitric oxide and ROS in cerebellar granule cells. Using selective enzyme inhibitors, it was shown that both protein kinase C and phospholipase A2 are involved in KCN-stimulated generation of NO and ROS. In cells **treated** with indomethacin or **nordihydroguaiaretic acid**, inhibitors of cyclooxygenase (COX) and lipoxygenase (LOX) respectively, attenuated (apprx35%) KCN-induced generation of oxidant species. When L-NAME (LG-nitro-L-arginine methyl ester) (nitric oxide synthase inhibitor, NOS) was combined with either indomethacin or **nordihydroguaiaretic acid**, generation of oxidant species was blocked by more than 80%. Pretreatment with NS398 (COX-2 inhibitor) significantly decreased ROS generation indicating the involvement of COX-2 in KCN-induced oxidant generation. **Treatment** with L-NAME + NS398 blocked oxidant species generation, reflecting involvement of NOS. The participation of cytochrome P450 was not evident because SKF525A did not significantly reduce KCN-induced ROS generation. Furthermore, a correlation was observed between oxidant generation and **lipid** peroxidation of cellular membranes (as determined by thiobarbituric acid levels). Pretreatment with inhibitors of protein kinase C, phospholipase A2 or COX, LOX, COX-2 partially blocked KCN-induced formation of thiobarbituric acid reactive substance, whereas coincubation of L-NAME with the inhibitors decreased **lipid** peroxidation by 60 to 90%. In cytotoxicity studies, KCN-induced cell death was partially blocked by the inhibitors and significant protection was observed when L-NAME was combined with these compounds. These findings show that activation of phospholipase A2 and subsequent metabolism of arachidonic acid by the COX-2 and LOX pathways and NOS contribute to cyanide-induced ROS

production.

AB. . . shown that both protein kinase C and phospholipase A2 are involved in KCN-stimulated generation of NO and ROS. In cells **treated** with indomethacin or **nordihydroguaiaretic acid**, inhibitors of cyclooxygenase (COX) and lipoxygenase (LOX) respectively, attenuated (apprx35%) KCN-induced generation of oxidant species. When L-NAME (LG-nitro-L-arginine methyl ester) (nitric oxide synthase inhibitor, NOS) was combined with either indomethacin or **nordihydroguaiaretic acid**, generation of oxidant species was blocked by more than 80%. Pretreatment with NS398 (COX-2 inhibitor) significantly decreased ROS generation indicating the involvement of COX-2 in KCN-induced oxidant generation. **Treatment** with L-NAME + NS398 blocked oxidant species generation, reflecting involvement of NOS. The participation of cytochrome P450 was not evident because SKF525A did not significantly reduce KCN-induced ROS generation. Furthermore, a correlation was observed between oxidant generation and **lipid** peroxidation of cellular membranes (as determined by thiobarbituric acid levels). Pretreatment with inhibitors of protein kinase C, phospholipase A2 or. . . COX, LOX, COX-2 partially blocked KCN-induced formation of thiobarbituric acid reactive substance, whereas coincubation of L-NAME with the inhibitors decreased **lipid** peroxidation by 60 to 90%. In cytotoxicity studies, KCN-induced cell death was partially blocked by the inhibitors and significant protection. . .

L8 ANSWER 42 OF 46 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1985:230129 BIOSIS
DOCUMENT NUMBER: BA79:10125
TITLE: NEUTROPHIL CHEMOTACTIC FACTOR PRODUCED BY ALVEOLAR MACROPHAGES IN-VITRO.
AUTHOR(S): KAWANO T
CORPORATE SOURCE: THIRD DEP. INTERN. MED., SCH. MED., UNIV. TOKUSHIMA, TOKUSHIMA.
SOURCE: SHIKOKU ACTA MED, (1983 (RECD 1984)) 39 (6), 567-579. CODEN: SKIZAB. ISSN: 0037-3699.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese

AB To clarify nature and pathophysiological significance of alveolar macrophages (AM)-produced neutrophil chemotactic factor (NCF), properties of the NCF produced by zymosan-stimulated rat and human AM in vitro. Rat and human AM were obtained by broncho-alveolar lavage and suspended in RPMI-1640 medium. Assay of chemotaxis was carried out by the method of Nelson et al using agarose plate. Properties of the NCF produced by rat AM in vitro were obtained. The AM were cultured at 37.degree. C in a CO2-incubator with or without zymosan. The AM released NCF in the culture medium only when incubated with zymosan. About 80% of the NCF was extracted with ether and the NCF was stable for heat **treatment**. Production of the NCF by AM was not inhibited by inhibitors of protein synthesis such as cycloheximide and actinomycin D, but inhibited by **nordihydroguaiaretic acid** (an inhibitor only of the lipoxygenase of arachidonate metabolism) or 5, 8, 11, 14 eicosatetraynoic acid (an inhibitor of both lipoxygenase and cyclooxygenase). The results of analysis of the ether-extractable NCF by thin layer chromatography and high performance liquid chromatography (HPLC) indicate that it corresponds to an arachidonate lipoxygenase product, especially leukotriene B4 (LTB). Evidently, 1 of the NCF produced by zymosan-stimulated rat AM is an arachidonate lipoxygenase product, LTB. In vitro production of NCF by zymosan-stimulated human AM was indicated. The human AM also produced NCF in the culture medium when cultured with zymosan. Amount of the NCF produced per cell was significantly smaller in the AM from smokers than in the AM from nonsmokers. Most of the NCF was extractable with ether. HPLC showed that the ether-extractable NCF also corresponds to LTB. AM may release a NCF with nature of **lipid** for stimuli, and the NCF play

some roles in defense mechanism and inflammation of the lung.
AB. . . when incubated with zymosan. About 80% of the NCF was extracted with ether and the NCF was stable for heat **treatment**. Production of the NCF by AM was not inhibited by inhibitors of protein synthesis such as cycloheximide and actinomycin D, but inhibited by **nordihydroguaiaretic acid** (an inhibitor only of the lipoxygenase of arachidonate metabolism) or 5, 8, 11, 14 eicosatetraynoic acid (an inhibitor of both. . . with ether. HPLC showed that the ether-extractable NCF also corresponds to LTB. AM may release a NCF with nature of **lipid** for stimuli, and the NCF play some roles in defense mechanism and inflammation of the lung.

```
=> s lipoxygenase
L9       39964 LIPOXYGENASE

=> s l6 (s) l9
L10        104 L6 (S) L9

=> focus
PROCESSING COMPLETED FOR L10
L11         104 FOCUS L10 1-

=> d ibib abs kwic 1-5

L11  ANSWER 1 OF 104     MEDLINE
ACCESSION NUMBER:   92248783     MEDLINE
DOCUMENT NUMBER:    92248783   PubMed ID: 1576704
TITLE:              Bioactivation of aflatoxin B1 by lipoxygenases,
                    prostaglandin H synthase and cytochrome P450 monooxygenase
                    in guinea-pig tissues.
AUTHOR:             Liu L; Massey T E
CORPORATE SOURCE:   Department of Pharmacology and Toxicology, Queen's
                    University, Kingston, Ontario, Canada.
SOURCE:             CARCINOGENESIS, (1992 Apr) 13 (4) 533-9.
                    Journal code: C9T; 8008055. ISSN: 0143-3334.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199206
ENTRY DATE:         Entered STN: 19920619
                    Last Updated on STN: 19970203
                    Entered Medline: 19920605
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AB In the present investigation, we have examined the role of **lipoxygenases** in the bioactivation of aflatoxin B1 (AFB1) in hepatic and extrahepatic tissues. The enzyme activities were evaluated by determining [3H]AFB1-DNA adduct formation. The results demonstrated that both purified soybean **lipoxygenase** and guinea-pig tissue cytosolic **lipoxygenases** were able to activate AFB1 to form [3H]AFB1-DNA adduct(s). The reaction was completely inhibited by **nordihydroguaiaretic acid** (**NDGA**, 0.1 mM), a **lipoxygenase** inhibitor and an antioxidant, but not by indomethacin (0.1 mM), an inhibitor of prostaglandin H synthase (PHS), indicating that this reaction is associated with **lipoxygenase** activity, and/or is involved in a peroxyl radical process. While purified **lipoxygenase** showed arachidonic acid (AA)-dependent properties, the omission of AA did not diminish guinea-pig tissue cytosolic [3H]AFB1-DNA adduct formation, possibly because AA was released from **lipid** particles by AFB1. Within the range of hemoglobin (Hb) concentrations found in lung, kidney and liver cytosols (1.4-11.1 microM) and microsomes (0-0.5 microM), neither pure Hb, nor Hb of cytosols or

microsomes from whole blood caused detectable AA-dependent AFB1-DNA binding. This indicates that Hb, as a contaminant with quasi-**lipoxygenase** activity, did not contribute to AFB1 activation attributed to guinea-pig tissue **lipoxygenases**. [3H]AFB1 concentrations at half-maximal DNA binding rate of pulmonary cytochrome P450 monooxygenases (P450) and **lipoxygenases** were similar, though P450 had a much higher maximum DNA binding rate. Pulmonary microsomal PHS activity for AFB1 activation was too low for its half-maximal binding concentrations of [3H]AFB1 and maximum rate to be accurately determined. In kidney, maximum rates for **lipoxygenase** , PHS and P450 were similar, whereas half-maximal binding concentrations for reactions by **lipoxygenase** and P450 were lower compared to that of PHS. The half-maximal binding concentration of hepatic **lipoxygenase** was significantly lower than those for PHS and P450. Hepatic half-maximal binding concentrations for PHS and P450 were similar, though P450 had a much higher maximum rate than PHS and **lipoxygenases**. These data suggest that **lipoxygenase** -catalyzed AFB1 activation can occur at low AFB1 concentrations. This may be important in view of human exposure to low AFB1 concentrations and predominant **lipoxygenase** activity in human airway epithelial cells. When expressed per gram of tissue, renal and hepatic PHS activities and renal **lipoxygenase** activities for AFB1 activation were similar, and higher than the activity of pulmonary PHS, while pulmonary PHS activity for the oxidation of N,N,N',N'-tetramethyl-p-phenylenediamine (TMPD) was similar to that in liver and lower than that in kidney.(ABSTRACT TRUNCATED AT 400 WORDS)

AB In the present investigation, we have examined the role of **lipoxygenases** in the bioactivation of aflatoxin B1 (AFB1) in hepatic and extrahepatic tissues. The enzyme activities were evaluated by determining [3H]AFB1-DNA adduct formation. The results demonstrated that both purified soybean **lipoxygenase** and guinea-pig tissue cytosolic **lipoxygenases** were able to activate AFB1 to form [3H]AFB1-DNA adduct(s). The reaction was completely inhibited by **nordihydroguaiaretic acid** (**NDGA**, 0.1 mM), a **lipoxygenase** inhibitor and an antioxidant, but not by indomethacin (0.1 mM), an inhibitor of prostaglandin H synthase (PHS), indicating that this reaction is associated with **lipoxygenase** activity, and/or is involved in a peroxyl radical process. While purified **lipoxygenase** showed arachidonic acid (AA)-dependent properties, the omission of AA did not diminish guinea-pig tissue cytosolic [3H]AFB1-DNA adduct formation, possibly because AA was released from **lipid** particles by AFB1. Within the range of hemoglobin (Hb) concentrations found in lung, kidney and liver cytosols (1.4-11.1 microM) and. . . of cytosols or microsomes from whole blood caused detectable AA-dependent AFB1-DNA binding. This indicates that Hb, as a contaminant with quasi-**lipoxygenase** activity, did not contribute to AFB1 activation attributed to guinea-pig tissue **lipoxygenases**. [3H]AFB1 concentrations at half-maximal DNA binding rate of pulmonary cytochrome P450 monooxygenases (P450) and **lipoxygenases** were similar, though P450 had a much higher maximum DNA binding rate. Pulmonary microsomal PHS activity for AFB1 activation was. . . low for its half-maximal binding concentrations of [3H]AFB1 and maximum rate to be accurately determined. In kidney, maximum rates for **lipoxygenase** , PHS and P450 were similar, whereas half-maximal binding concentrations for reactions by **lipoxygenase** and P450 were lower compared to that of PHS. The half-maximal binding concentration of hepatic **lipoxygenase** was significantly lower than those for PHS and P450. Hepatic half-maximal binding concentrations for PHS and P450 were similar, though P450 had a much higher maximum rate than PHS and **lipoxygenases**. These data suggest that **lipoxygenase** -catalyzed AFB1 activation can occur at low AFB1 concentrations. This may be important in view of human exposure to low AFB1 concentrations and

predominant **lipoxygenase** activity in human airway epithelial cells. When expressed per gram of tissue, renal and hepatic PHS activities and renal **lipoxygenase** activities for AFB1 activation were similar, and higher than the activity of pulmonary PHS, while pulmonary PHS activity for the. . .

L11 ANSWER 2 OF 104 MEDLINE
ACCESSION NUMBER: 97219351 MEDLINE
DOCUMENT NUMBER: 97219351 PubMed ID: 9066651
TITLE: Proliferative responses of normal human mammary and MCF-7 breast cancer cells to linoleic acid, conjugated linoleic acid and eicosanoid synthesis inhibitors in culture.
AUTHOR: Cunningham D C; Harrison L Y; Shultz T D
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Washington State University, Pullman 99164-6376, USA.
SOURCE: ANTICANCER RESEARCH, (1997 Jan-Feb) 17 (1A) 197-203. Journal code: 59L; 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970422
Last Updated on STN: 19980206
Entered Medline: 19970407

AB Potential mechanisms for the stimulation or inhibition of cell growth by linoleic acid (LA) and conjugated linoleic acid (CLA) were investigated by using eicosanoid synthesis inhibitors. Normal human mammary epithelial cells (HMEC) and MCF-7 breast cancer cells were incubated in serum-free medium supplemented with LA or CLA and cyclooxygenase (indomethacin; INDO) or **lipoxygenase (nordihydroguaiaretic acid; NDGA**) inhibitors. Linoleic acid stimulated the growth and [3H]thymidine incorporation of normal HMEC and MCF-7 cancer cells, while CLA was inhibitory. Supplementation with LA increased intracellular **lipid** peroxide concentrations in normal HMEC and MCF-7 cancer cells, whereas CLA did not affect **lipid** peroxide formation. Normal HMEC and MCF-7 cells supplemented with LA and INDO or **NDGA** resulted in growth inhibition. The treatment of normal HMEC with CLA and INDO or **NDGA**, and MCF-7 cells with CLA and INDO stimulated cell growth. However, the addition of CLA and **NDGA** to MCF-7 cells resulted in synergistic growth suppression suggesting that CLA effects were mediated through **lipoxygenase** inhibition. Although **NDGA** was more inhibitory of cell growth in the presence of LA or CLA than INDO, growth was associated with both prostaglandin and leukotriene production. Additional studies are warranted to elucidate the mechanism(s) whereby LA or CLA affect breast cell growth.

AB . . . and MCF-7 breast cancer cells were incubated in serum-free medium supplemented with LA or CLA and cyclooxygenase (indomethacin; INDO) or **lipoxygenase (nordihydroguaiaretic acid; NDGA**) inhibitors. Linoleic acid stimulated the growth and [3H]thymidine incorporation of normal HMEC and MCF-7 cancer cells, while CLA was inhibitory. Supplementation with LA increased intracellular **lipid** peroxide concentrations in normal HMEC and MCF-7 cancer cells, whereas CLA did not affect **lipid** peroxide formation. Normal HMEC and MCF-7 cells supplemented with LA and INDO or **NDGA** resulted in growth inhibition. The treatment of normal HMEC with CLA and INDO or **NDGA**, and MCF-7 cells with CLA and INDO stimulated cell growth. However, the addition of CLA and **NDGA** to MCF-7 cells resulted in synergistic growth suppression suggesting that CLA effects were mediated through **lipoxygenase** inhibition. Although **NDGA** was more inhibitory of cell growth in the presence of LA or CLA than INDO, growth was associated with both. . .

L11 ANSWER 3 OF 104 MEDLINE
ACCESSION NUMBER: 93049813 MEDLINE
DOCUMENT NUMBER: 93049813 PubMed ID: 1426000
TITLE: Effects of baicalein and alpha-tocopherol on lipid peroxidation, free radical scavenging activity and 12-O-tetradecanoylphorbol acetate-induced ear edema.
AUTHOR: Hara H; Sukamoto T; Ohtaka H; Abe K; Tatumi Y; Saito Y; Suzuki A; Tsukamoto G
CORPORATE SOURCE: Department of Pharmacology, Kanebo Ltd., Osaka, Japan.
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1992 Oct 20) 221 (2-3) 193-8.
Journal code: EN6; 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921222

AB The effects of baicalein, a flavonoid, and alpha-tocopherol (vitamin E) on **lipid** peroxidation in rat forebrain homogenates, on free radical scavenging action against diphenyl-p-picrylhydrazyl (DPPH), and on 12-O-tetradecanoylphorbol acetate (TPA)-induced ear edema in mice were studied. Baicalein inhibited **lipid** peroxidation in forebrain homogenates, DPPH-induced free radical and TPA-induced ear edema as potently as did quercetin and **nordihydroguaiaretic acid (NDGA)**, a **lipoxygenase** inhibitor, and more potently than BW755C, a mixed cyclooxygenase and **lipoxygenase** inhibitor. **Lipid** peroxidation in forebrain homogenates, DPPH-induced free radical and TPA-induced ear edema were also inhibited by alpha-tocopherol. Flavone showed no reaction. These results suggest that **lipid** peroxidation may play an important role in the pathogenesis of TPA-induced ear edema in mice.
AB The effects of baicalein, a flavonoid, and alpha-tocopherol (vitamin E) on **lipid** peroxidation in rat forebrain homogenates, on free radical scavenging action against diphenyl-p-picrylhydrazyl (DPPH), and on 12-O-tetradecanoylphorbol acetate (TPA)-induced ear edema in mice were studied. Baicalein inhibited **lipid** peroxidation in forebrain homogenates, DPPH-induced free radical and TPA-induced ear edema as potently as did quercetin and **nordihydroguaiaretic acid (NDGA)**, a **lipoxygenase** inhibitor, and more potently than BW755C, a mixed cyclooxygenase and **lipoxygenase** inhibitor. **Lipid** peroxidation in forebrain homogenates, DPPH-induced free radical and TPA-induced ear edema were also inhibited by alpha-tocopherol. Flavone showed no reaction. These results suggest that **lipid** peroxidation may play an important role in the pathogenesis of TPA-induced ear edema in mice.

L11 ANSWER 4 OF 104 MEDLINE
ACCESSION NUMBER: 92187611 MEDLINE
DOCUMENT NUMBER: 92187611 PubMed ID: 1546066
TITLE: Activation of 15-lipoxygenase by low density lipoprotein in vascular endothelial cells. Relationship to the oxidative modification of low density lipoprotein.
AUTHOR: Derian C K; Lewis D F
CORPORATE SOURCE: Department of Cardiovascular Pharmacology, Rhone-Poulenc Rorer Central Research, King of Prussia, Pennsylvania 19406.
SOURCE: PROSTAGLANDINS LEUKOTRIENES AND ESSENTIAL FATTY ACIDS, (1992 Jan) 45 (1) 49-57.

Journal code: P04; 8802730. ISSN: 0952-3278.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 19920424
Last Updated on STN: 19980206
Entered Medline: 19920410

AB Oxidatively-modified low density lipoprotein (LDL) is thought to play a significant role in the formation of **lipid**-laden macrophages, the primary cellular component of atherosclerotic fatty lesions. Recently, **lipoxygenases** have been implicated as a major enzymatic pathway involved in rabbit endothelial cell-mediated LDL modification. We investigated the effect of LDL on porcine aortic endothelial cell (PAEC) and human umbilical vein (HUVEC) and aortic endothelial cell (HAEC) **lipoxygenase** activity. By thin layer chromatography, we observed that human LDL stimulated the metabolism of radiolabeled arachidonic acid to 12 + 15-hydroxyeicosatetraenoic acid (HETE) in indomethacin-treated PAEC. Furthermore, radiolabeled linoleic acid, a specific substrate for the 15-**lipoxygenase**, was metabolized to its respective product 13-hydroxyoctadecadienoic acid (13-HODE) in the presence of LDL. Increased product formation in both studies was inhibited by the **lipoxygenase** blockers **nordihydroguaiaretic acid** (**NDGA**) and RG 6866. 15-HETE was confirmed as the predominant HETE product in LDL-treated cells by high performance liquid chromatography. Both porcine- and human-derived LDL stimulated the CL release of 15-HETE from cells as determined by radioimmunoassay. Release of immunoreactive 15-HETE was inhibited by **NDGA**, RG 6866, and 5,8,11,14-eicosatetraynoic acid (ETYA) but not by the selective 5-**lipoxygenase** inhibitor RG 5901. These **lipoxygenase** inhibitors had similar effects on the modification of LDL. Our results suggest that the oxidative modification of LDL by endothelial cells may be mediated in part through activation of 15-**lipoxygenase**.

AB Oxidatively-modified low density lipoprotein (LDL) is thought to play a significant role in the formation of **lipid**-laden macrophages, the primary cellular component of atherosclerotic fatty lesions. Recently, **lipoxygenases** have been implicated as a major enzymatic pathway involved in rabbit endothelial cell-mediated LDL modification. We investigated the effect of LDL on porcine aortic endothelial cell (PAEC) and human umbilical vein (HUVEC) and aortic endothelial cell (HAEC) **lipoxygenase** activity. By thin layer chromatography, we observed that human LDL stimulated the metabolism of radiolabeled arachidonic acid to 12 + 15-hydroxyeicosatetraenoic acid (HETE) in indomethacin-treated PAEC. Furthermore, radiolabeled linoleic acid, a specific substrate for the 15-**lipoxygenase**, was metabolized to its respective product 13-hydroxyoctadecadienoic acid (13-HODE) in the presence of LDL. Increased product formation in both studies was inhibited by the **lipoxygenase** blockers **nordihydroguaiaretic acid** (**NDGA**) and RG 6866. 15-HETE was confirmed as the predominant HETE product in LDL-treated cells by high performance liquid chromatography. Both. . . LDL stimulated the CL release of 15-HETE from cells as determined by radioimmunoassay. Release of immunoreactive 15-HETE was inhibited by **NDGA**, RG 6866, and 5,8,11,14-eicosatetraynoic acid (ETYA) but not by the selective 5-**lipoxygenase** inhibitor RG 5901. These **lipoxygenase** inhibitors had similar effects on the modification of LDL. Our results suggest that the oxidative modification of LDL by endothelial cells may be mediated in part through activation of 15-**lipoxygenase**.

L11 ANSWER 5 OF 104 MEDLINE
ACCESSION NUMBER: 91139676 MEDLINE

DOCUMENT NUMBER: 91139676 PubMed ID: 1899867
TITLE: Endogenous non-cyclooxygenase metabolites of arachidonic acid modulate growth and mRNA levels of immediate-early response genes in rat mesangial cells.
AUTHOR: Sellmayer A; Uedelhoven W M; Weber P C; Bonventre J V
CORPORATE SOURCE: Department of Medicine, Harvard Medical School, Boston, Massachusetts.
CONTRACT NUMBER: DK 38165 (NIDDK)
DK 38452 (NIDDK)
DK 39773 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Feb 25) 266 (6) 3800-7.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 20000303
Entered Medline: 19910327

AB The role of endogenous arachidonic acid and its metabolites as mediators of cell growth was studied in rat mesangial cells. Inhibitors of the cytochrome P450 monooxygenase and **lipoxygenase** systems (**nordihydroguaiaretic acid** (**NDGA**), SK&F 525A, and ketoconazole) significantly reduced serum-stimulated cell growth as determined by cell counts and incorporation of [3H]thymidine. Inhibition of cyclooxygenase or **lipoxygenases** alone had no effect on cell growth. Stimulation with arginine vasopressin, epidermal growth factor, or phorbol myristate acetate increased [3H]thymidine incorporation and mRNA levels of the immediate-early response genes c-fos and Egr-1. These increases in [3H]thymidine incorporation and mRNA levels were reduced by **NDGA** and ketoconazole. **NDGA**, SK&F 525A, and ketoconazole had no effect on cellular ATP levels. Indomethacin had no effect upon cell growth. 14,15-Epoxyeicosatrienoic acid potentiated the effect of arginine vasopressin to enhance [3H]thymidine incorporation. Reverse-phase high pressure liquid chromatography analysis of **lipid** extracts from cells prelabeled with [3H]arachidonic acid resulted in the detection of a radioactive peak which eluted with **lipoxygenase** and monooxygenase products, with the same retention time as vicinal dihydroxyeicosatrienoic acids. This peak increased after stimulation with arginine vasopressin or epidermal growth factor and was reduced by preincubation with **NDGA**. Furthermore, analysis of unlabeled cell extracts by gas chromatography-mass spectrometry revealed the presence of a compound with epoxyeicosatrienoic acid-like characteristics. These results indicate that mesangial cells in culture likely produce products of the cytochrome P450 monooxygenase system that are important endogenous mediators of the growth response to mitogenic agents.

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vasopressin to enhance [3H]thymidine incorporation. Reverse-phase high pressure liquid chromatography analysis of **lipid** extracts from cells prelabeled with [3H]arachidonic acid resulted in the detection of a radioactive peak which eluted with **lipoxygenase** and monooxygenase products, with the same retention time as vicinal dihydroxyeicosatrienoic acids. This peak increased after stimulation with arginine vasopressin or epidermal growth factor and was reduced by preincubation with **NDGA**. Furthermore, analysis of unlabeled cell extracts by gas chromatography-mass spectrometry revealed the presence of a compound with epoxyeicosatrienoic acid-like characteristics.. . .

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L11 ANSWER 6 OF 104 MEDLINE
ACCESSION NUMBER: 1998200679 MEDLINE
DOCUMENT NUMBER: 98200679 PubMed ID: 9539859
TITLE: Lipid peroxidation, arachidonic acid and products of the lipoxygenase pathway in ischaemic preconditioning of rat heart.
AUTHOR: Starkopf J; Andreasen T V; Bugge E; Ytrehus K
CORPORATE SOURCE: Department of Biochemistry, Faculty of Medicine, University of Tartu, Estonia.. joels@fagmed.uit.no
SOURCE: CARDIOVASCULAR RESEARCH, (1998 Jan) 37 (1) 66-75.
Journal code: COR; 0077427. ISSN: 0008-6363.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416

AB OBJECTIVE: Preconditioning with brief intermittent periods of ischaemia is known to provide protection against ischaemic injury. It has been suggested that myocardial ischaemia also activates phospholipase A2, which releases arachidonic acid from phospholipids. In the present study the possible role of phospholipid peroxidation, arachidonic acid and products of the **lipoxygenase** pathway in cellular mechanisms of ischaemic preconditioning was examined. METHODS: Isolated, buffer-perfused rat hearts were freeze-clamped at the end of preconditioning (a cycle of 5 min global ischaemia +5 min reperfusion) and at the end of 30 min global ischaemia and analysed for non-esterified fatty acids and fatty acids in the 2-position of phospholipid. In a separate set of experiments, hearts pretreated with a **lipoxygenase** inhibitor, **nordihydroguaiaretic acid** (**NDGA**), were subjected to 30 min regional ischaemia and 120 min reperfusion. Infarct size was determined by tetrazolium staining and the ischaemic risk zone with fluorescent particles. RESULTS: Myocardial levels of arachidonic as well as of linoleic and docosahexaenoic acid were significantly elevated by preconditioning. Also, the level of peroxidized polyunsaturated fatty acids (measured as hydroxy conjugated dienes) in myocardial phospholipid was significantly increased: 101.4 +/- 16.8 nmol/g versus 51.2 +/- 7.3 nmol/g tissue dw in the control group, $p < 0.05$. Pre-treatment of hearts with 5 microM **NDGA** blocked the infarct limiting effects of preconditioning: infarct size was 37.4 +/- 6.4% of risk zone in control, 9.0 +/- 0.9% in the preconditioning group and 27.7 +/- 3.8% in the preconditioning + **NDGA** group ($p < 0.05$ vs. i.p., n.s. vs. control). CONCLUSION: Our findings provide evidence for the involvement of phospholipase A2 and **lipoxygenase** derived **lipid** second messengers in ischaemic preconditioning of the isolated rat heart.

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possible role of phospholipid peroxidation, arachidonic acid and products of the **lipoxygenase** pathway in cellular mechanisms of ischaemic preconditioning was examined. METHODS: Isolated, buffer-perfused rat hearts were freeze-clamped at the end of. . . fatty acids and fatty acids in the 2-position of phospholipid. In a separate set of experiments, hearts pretreated with a **lipoxygenase** inhibitor, **nordihydroguaiaretic acid** (**NDGA**), were subjected to 30 min regional ischaemia and 120 min reperfusion. Infarct size was determined by tetrazolium staining and the. . . versus 51.2 +/- 7.3 nmol/g tissue dw in the control group, $p < 0.05$. Pre-treatment of hearts with 5 microM **NDGA** blocked the infarct limiting effects of preconditioning: infarct size was 37.4 +/- 6.4% of risk zone in control, 9.0 +/- 0.9% in the preconditioning group and 27.7 +/- 3.8% in the preconditioning + **NDGA** group ($p < 0.05$ vs. i.p., n.s. vs. control). CONCLUSION: Our findings provide evidence for the involvement of phospholipase A2 and **lipoxygenase** derived **lipid** second messengers in ischaemic preconditioning of the isolated rat heart.

L11 ANSWER 7 OF 104 MEDLINE
ACCESSION NUMBER: 2001488497 MEDLINE
DOCUMENT NUMBER: 21422061 PubMed ID: 11531219
TITLE: The role of eicosanoids in the process of adaptation following massive bowel resection in the rat.
AUTHOR: Kollman-Bauerly K A; Thomas D L; Adrian T E; Lien E L; Vanderhoof J A
CORPORATE SOURCE: Department of Pediatrics, University of Nebraska Medical Center/Creighton University, Omaha, USA.
SOURCE: JPEN. JOURNAL OF PARENTERAL AND ENTERAL NUTRITION, (2001 Sep-Oct) 25 (5) 275-81.
Journal code: 7804134. ISSN: 0148-6071.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20010904
Last Updated on STN: 20020125
Entered Medline: 20020122

AB BACKGROUND: Long chain polyunsaturated fatty acids (LCPUFAs) such as arachidonic acid (AA) and eicosapentaenoic acid (EPA) stimulate intestinal adaptation. Prostaglandins also enhance intestinal adaptation. The purpose of this study was to determine by which eicosanoid pathway dietary arachidonic acid enhances intestinal adaptation. Cyclo-oxygenase or **lipoxygenase** were selectively inhibited to determine whether either of them enhanced or inhibited adaptation. METHODS: Sixty Sprague-Dawley rats were divided into 2 groups, one receiving an 80% small bowel resection and the other receiving a sham operation. Rats were further divided into groups receiving either a placebo, a general **lipoxygenase** inhibitor (**nordihydroguaiaretic acid** [**NDGA**] at 40 mg/kg per day), or a cyclo-oxygenase-2 inhibitor (Etodolac at 3 mg/kg per day). Rats were pair-fed a diet containing 30% kcal from **fat**, primarily consisting of AA. RESULTS: After 14 days, mucosal mass, protein, DNA, and disaccharidase activity were measured in the remaining small intestine. There was a significant decrease in ileal mucosal mass in rats receiving Etodolac and a significant increase in mucosal mass in the duodenum in rats receiving **NDGA** (both $p < .001$). Mucosal DNA, protein, and disaccharidase data showed similar trends. CONCLUSIONS: These findings suggest that after small bowel resection, dietary arachidonic acid may facilitate the adaptation process by acting as a substrate for the synthesis of prostaglandins, and not through the derivatives of **lipoxygenase** such as leukotrienes or thromboxanes.

AB . . . The purpose of this study was to determine by which eicosanoid pathway dietary arachidonic acid enhances intestinal adaptation. Cyclo-oxygenase or **lipoxygenase** were selectively inhibited to determine whether either of them enhanced or inhibited adaptation. METHODS: Sixty Sprague-Dawley rats were divided into. . . resection and the other receiving a sham operation. Rats were further divided into groups receiving either a placebo, a general **lipoxygenase** inhibitor (**nordihydroguaiaretic acid [NDGA]** at 40 mg/kg per day), or a cyclo-oxygenase-2 inhibitor (Etodolac at 3 mg/kg per day). Rats were pair-fed a diet containing 30% kcal from **fat**, primarily consisting of AA. RESULTS: After 14 days, mucosal mass, protein, DNA, and disaccharidase activity were measured in the remaining. . . ileal mucosal mass in rats receiving Etodolac and a significant increase in mucosal mass in the duodenum in rats receiving **NDGA** (both $p < .001$). Mucosal DNA, protein, and disaccharidase data showed similar trends. CONCLUSIONS: These findings suggest that after small. . . facilitate the adaptation process by acting as a substrate for the synthesis of prostaglandins, and not through the derivatives of **lipoxygenase** such as leukotrienes or thromboxanes.

L11 ANSWER 8 OF 104 MEDLINE
ACCESSION NUMBER: 2000270661 MEDLINE
DOCUMENT NUMBER: 20270661 PubMed ID: 10810364
TITLE: Lipid peroxidation is associated with the inhibitory action of all-trans-retinoic acid on mammary cell transformation.
AUTHOR: Kubow S; Woodward T L; Turner J D; Nicodemo A; Long E; Zhao X
CORPORATE SOURCE: School of Dietetics and Human Nutrition, McGill University, Ste. Anne de Bellevue, Quebec, Canada.. Kubow@agradm.lan.mcgill.ca
SOURCE: ANTICANCER RESEARCH, (2000 Mar-Apr) 20 (2A) 843-8. Journal code: 59L; 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000613
Last Updated on STN: 20000613
Entered Medline: 20000601

AB BACKGROUND: Retinoids are effective in reducing transformation of various cell types; however the role of **lipid** peroxidation has not been studied in this regard. MATERIALS AND METHODS: Retinoic acid (RA) and retinol were tested on several SV-40 large-T-antigen transformed bovine mammary fibroblast (MFB) lines that form foci on plastic with long-term culture. RESULTS: Dose response studies revealed that RA at 10(-6) M was the most potent dose in delaying the onset of foci formation and reducing total foci number. RA was always more effective than retinol. Addition of RA (10(-6) M) to MFB cells increased **lipid** peroxide (LPO) concentrations by approximately three-fold relative to untreated MFB cells or to RA or control treated normal mammary fibroblasts. The **lipoxygenase** inhibitor, **nordihydroguaiaretic acid (NDGA)**, acted synergistically with RA to increase LPO and cell death in MFB cells. The combination of the cyclooxygenase inhibitor, indomethacin, at 10(-4) M with 10(-6) M RA lowered MFB fibroblast cell numbers when compared to fibroblasts cultured singly with either RA or indomethacin. CONCLUSIONS: These data indicate that an increase in **lipid** peroxidation occurs specifically in tumor cells treated with RA and this may play a role in RA-mediated suppression of cellular transformation in the mammary gland. Additionally, eicosanoid inhibitors may have an additive or synergistic effect with RA on the inhibition of mammary tumor cell transformation and proliferation.

AB BACKGROUND: Retinoids are effective in reducing transformation of various cell types; however the role of **lipid** peroxidation has not been studied in this regard. MATERIALS AND METHODS: Retinoic acid (RA) and retinol were tested on several. . . reducing total foci number. RA was always more effective than retinol. Addition of RA (10(-6) M) to MFB cells increased **lipid** peroxide (LPO) concentrations by approximately three-fold relative to untreated MFB cells or to RA or control treated normal mammary fibroblasts. The **lipoxygenase** inhibitor, **nordihydroguaiaretic acid** (**NDGA**), acted synergistically with RA to increase LPO and cell death in MFB cells. The combination of the cyclooxygenase inhibitor, indomethacin,. . . numbers when compared to fibroblasts cultured singly with either RA or indomethacin. CONCLUSIONS: These data indicate that an increase in **lipid** peroxidation occurs specifically in tumor cells treated with RA and this may play a role in RA-mediated suppression of cellular. . .

L11 ANSWER 9 OF 104 MEDLINE
ACCESSION NUMBER: 2000117249 MEDLINE
DOCUMENT NUMBER: 20117249 PubMed ID: 10653524
TITLE: Glutathione oxidation and mitochondrial depolarization as mechanisms of nordihydroguaiaretic acid-induced apoptosis in lipoxygenase-deficient FL5.12 cells.
AUTHOR: Biswal S S; Datta K; Shaw S D; Feng X; Robertson J D; Kehrer J P
CORPORATE SOURCE: Division of Pharmacology and Toxicology, College of Pharmacy, The University of Texas at Austin, 78712-1074, USA.
CONTRACT NUMBER: ES07784 (NIEHS)
HL48035 (NHLBI)
HL51005 (NHLBI)
SOURCE: TOXICOLOGICAL SCIENCES, (2000 Jan) 53 (1) 77-83.
Journal code: CZ1; 9805461. ISSN: 1096-6080.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000215

AB **Nordihydroguaiaretic acid** (**NDGA**) induces apoptosis in a variety of cell lines. The mechanism(s) of this effect is not known, although the focus has been on the ability of **NDGA** to inhibit **lipoxygenase** (LOX) activities. In the present study, **NDGA**-induced apoptosis was studied in a murine hematopoietic cell line, FL5.12. Although this cell line lacks detectable LOX protein or activities, **NDGA** (10 microM) was able to induce apoptosis. There was a massive loss of mitochondrial membrane potential by 4 h after the addition of **NDGA**, suggesting that this organelle might be targeted by **NDGA**. A pro-oxidant **NDGA** effect has been suggested as playing a role in apoptosis. This was supported by the findings that glutathione disulfide levels were increased by 4 h following treatment with 10 microM **NDGA**, that pretreatment with N-acetylcysteine completely blocked the **NDGA**-induced loss of membrane potential and apoptosis, and that **lipid** peroxidation was enhanced in cells treated with **NDGA**. However, no evidence of increased levels of reactive oxygen could be seen in **NDGA** -treated cells loaded with dichlorofluorescin diacetate or dihydrorhodamine and analyzed by flow cytometry. Bcl-X(L) protein levels were unaffected by **NDGA** treatment. Caspase-3 was rapidly activated with a peak at 8 h after FL5.12 cells were treated with **NDGA**. Ac-DEVD-CHO (25 microM) and boc-asp-FMK (20 microM) both

inhibited caspase-3 enzyme activity by 97% 8 h after **NDGA** treatment. Boc-asp-FMK, a more general caspase inhibitor, delayed **NDGA**-induced apoptosis while Ac-DEVD-CHO, a more specific inhibitor of caspase-3, had no effect. These results suggest that **NDGA**-induced apoptosis happens through reactions that depolarize mitochondria, oxidize glutathione and **lipids**, but do not generate significant amounts of free reactive oxygen species.

AB **Nordihydroguaiaretic acid** (**NDGA**) induces apoptosis in a variety of cell lines. The mechanism(s) of this effect is not known, although the focus has been on the ability of **NDGA** to inhibit **lipoxygenase** (LOX) activities. In the present study, **NDGA**-induced apoptosis was studied in a murine hematopoietic cell line, FL5.12. Although this cell line lacks detectable LOX protein or activities, **NDGA** (10 microM) was able to induce apoptosis. There was a massive loss of mitochondrial membrane potential by 4 h after the addition of **NDGA**, suggesting that this organelle might be targeted by **NDGA**. A pro-oxidant **NDGA** effect has been suggested as playing a role in apoptosis. This was supported by the findings that glutathione disulfide levels were increased by 4 h following treatment with 10 microM **NDGA**, that pretreatment with N-acetylcysteine completely blocked the **NDGA**-induced loss of membrane potential and apoptosis, and that **lipid** peroxidation was enhanced in cells treated with **NDGA**. However, no evidence of increased levels of reactive oxygen could be seen in **NDGA** -treated cells loaded with dichlorofluorescin diacetate or dihydrorhodamine and analyzed by flow cytometry. Bcl-X(L) protein levels were unaffected by **NDGA** treatment. Caspase-3 was rapidly activated with a peak at 8 h after FL5.12 cells were treated with **NDGA**. Ac-DEVD-CHO (25 microM) and boc-asp-FMK (20 microM) both inhibited caspase-3 enzyme activity by 97% 8 h after **NDGA** treatment. Boc-asp-FMK, a more general caspase inhibitor, delayed **NDGA**-induced apoptosis while Ac-DEVD-CHO, a more specific inhibitor of caspase-3, had no effect. These results suggest that **NDGA**-induced apoptosis happens through reactions that depolarize mitochondria, oxidize glutathione and **lipids**, but do not generate significant amounts of free reactive oxygen species.

L11 ANSWER 10 OF 104 MEDLINE
ACCESSION NUMBER: 91117834 MEDLINE
DOCUMENT NUMBER: 91117834 PubMed ID: 1980544
TITLE: Intestinal motility disorder induced by peroxides: possible role of lipid peroxidation.
AUTHOR: Van der Vliet A; Tuinstra T J; Rademaker B; Bast A
CORPORATE SOURCE: Department of Pharmacochemistry, Faculty of Chemistry, Vrije Universiteit, Amsterdam, The Netherlands.
SOURCE: RESEARCH COMMUNICATIONS IN CHEMICAL PATHOLOGY AND PHARMACOLOGY, (1990 Nov) 70 (2) 227-43.
Journal code: R62; 0244734. ISSN: 0034-5164.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 19950206
Entered Medline: 19910304

AB The effect of oxidative stress on the rat small intestine was investigated by pretreatment of isolated segments from the jejunum with hydrogen peroxide or cumene hydroperoxide. Both peroxides induced responses in the small intestine, viz. a contraction followed by a slow relaxation. The contraction could be blocked by the cyclooxygenase inhibitor indomethacin and the phospholipase A2 inhibitor quinacrine, suggesting a role for

prostaglandins in the response. Pretreatment of intestinal segments with the peroxides diminished the muscarinic cholinergic response to methacholine. The **lipoxygenase** inhibitor **nordihydroguaiaretic acid** (**NDGA**) and the antioxidant butylated hydroxytoluene (BHT) both protected against the damage induced by cumene hydroperoxide, but did not influence the effect of hydrogen peroxide on the muscarinic response. In contrast to hydrogen peroxide, cumene hydroperoxide induced **lipid** peroxidation in intestinal membranes, which could also be blocked by **NDGA** or BHT. We conclude that cumene hydroperoxide alters the muscarinic response in the rat jejunum by the induction of **lipid** peroxidation, whereas the damage by hydrogen peroxide is probably induced intracellularly.

AB . . . for prostaglandins in the response. Pretreatment of intestinal segments with the peroxides diminished the muscarinic cholinergic response to methacholine. The **lipoxygenase** inhibitor **nordihydroguaiaretic acid** (**NDGA**) and the antioxidant butylated hydroxytoluene (BHT) both protected against the damage induced by cumene hydroperoxide, but did not influence the effect of hydrogen peroxide on the muscarinic response. In contrast to hydrogen peroxide, cumene hydroperoxide induced **lipid** peroxidation in intestinal membranes, which could also be blocked by **NDGA** or BHT. We conclude that cumene hydroperoxide alters the muscarinic response in the rat jejunum by the induction of **lipid** peroxidation, whereas the damage by hydrogen peroxide is probably induced intracellularly.

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=> fil stng
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              43.03      43.97

FILE 'STNGUIDE' ENTERED AT 18:44:08 ON 16 MAY 2002
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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               1.50      45.47

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 10, 2002 (20020510/UP).

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               1.14      46.61

FILE 'STNGUIDE' ENTERED AT 19:10:26 ON 16 MAY 2002
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LAST RELOADED: May 10, 2002 (20020510/UP).

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=> fil stng
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.56	48.17

FILE 'STNGUIDE' ENTERED AT 19:25:48 ON 16 MAY 2002
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 10, 2002 (20020510/UP).

=> log h
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.84	49.01

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 19:34:26 ON 16 MAY 2002

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FILE 'HOME' ENTERED AT 22:26:50 ON 13 MAY 2002

=> fil medl

=> s ?obes? or weight gain or weight loss or overweigh?
        157013 ?OBES?
        481023 WEIGHT
         39371 WEIGHTS
        494146 WEIGHT
                 (WEIGHT OR WEIGHTS)
         55665 GAIN
         10367 GAINS
         63484 GAIN
                 (GAIN OR GAINS)
         23163 WEIGHT GAIN
                 (WEIGHT(W)GAIN)
        481023 WEIGHT
         39371 WEIGHTS
        494146 WEIGHT
                 (WEIGHT OR WEIGHTS)
        258169 LOSS
         18443 LOSSES
        269951 LOSS
                 (LOSS OR LOSSES)
         22076 WEIGHT LOSS
                 (WEIGHT(W)LOSS)
          6323 OVERWEIGH?
L1      194642 ?OBES? OR WEIGHT GAIN OR WEIGHT LOSS OR OVERWEIGH?

=> s lipoxygenase
          9921 LIPOXYGENASE
          1310 LIPOXYGENASES
L2        10042 LIPOXYGENASE
                 (LIPOXYGENASE OR LIPOXYGENASES)

=> s l1 and l2
L3           87 L1 AND L2

=> s l1 (S) l2
L4           56 L1 (S) L2

=> d ibib abs kwic 50-56

L4   ANSWER 50 OF 56     MEDLINE
Full Text
ACCESSION NUMBER:   85203738     MEDLINE
DOCUMENT NUMBER:    85203738   PubMed ID: 3922746
TITLE:              Involvement of eicosanoids in release of oxytocin and
                    vasopressin from the neural lobe of the rat pituitary.
AUTHOR:             Negro-Vilar A; Snyder G D; Falck J R; Manna S; Chacos N;
                    Capdevila J
CONTRACT NUMBER:    HD-09988-3 (NICHD)
                    HD-15465 (NICHD)
                    NIGMS 31278 (NIGMS)
SOURCE:             ENDOCRINOLOGY, (1985 Jun) 116 (6) 2663-8.
                    Journal code: EGZ; 0375040. ISSN: 0013-7227.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        198507
ENTRY DATE:         Entered STN: 19900320
                    Last Updated on STN: 19970203
                    Entered Medline: 19850710
AB   Arachidonic acid (AA) is oxidized via three pathways which result in
     several series of distinct metabolites. Cyclooxygenase produces
     prostaglandins (PGs), prostacyclins, and thromboxanes. Lipoxygenase
     produces hydroperoxy/hydroxyeicosatetraenoic acids (HPETE/HETEs) and
     leukotrienes. Epoxygenase, a recently uncovered pathway, results in
     epoxyeicosatrienoic acids (EETs). Based on reverse phase HPLC product
     analysis, this study establishes that all three pathways of AA metabolism
     are present in microsomal incubates of the neural lobe of the pituitary
     gland. Addition of PGE2 to incubated fragments of neural lobes of the
     rat pituitary stimulates secretion of both arginine vasopressin (AVP) and
```

oxytocin in vitro. Inclusion of 5-HETE and 12-HETE in the incubation medium stimulates marginal release of AVP and oxytocin by 12-HETE only. The magnitude of AVP and oxytocin secretion stimulated by the epoxygenase metabolites 8,9-, 11,12-, and 14,15-EET is equal to that caused by PGE2. Maximal stimulation of secretion (3- to 4-fold) requires an EET concentration 10-15 times greater than that of PGE2. In contrast, 5,6-EET is inactive. These data suggest that oxygenated products of AA play a role in AVP and oxytocin secretion. Although PGs appear to be the dominant arachidonate metabolites involved in the release of AVP and oxytocin, the EETs probably have a contributing role.

L4 ANSWER 51 OF 56 MEDLINE
Full Text
ACCESSION NUMBER: 85188551 MEDLINE
DOCUMENT NUMBER: 85188551 PubMed ID: 2986027
TITLE: Modification of basal and GRF-stimulated cyclic AMP levels and growth hormone release by phospholipid metabolic enzyme inhibitors.
AUTHOR: Cronin M J; MacLeod R M; Canonico P L
CONTRACT NUMBER: 1K04NS00601 (NINDS)
AM-22125 (NIADDK)
NS32632 (NINDS)
+
SOURCE: NEUROENDOCRINOLOGY, (1985 Apr) 40 (4) 332-8.
Journal code: NY8; 0035665. ISSN: 0028-3835.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198506
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850617

AB The relative importance of several phospholipid pathways in cyclic AMP (cAMP) metabolism and growth hormone (GH) release was determined by an indirect, pharmacological approach in cultured anterior pituitary cells. The diglyceride lipase inhibitor RHC-80267 (30-100 microM) had no significant effect on cAMP levels but markedly inhibited basal and growth hormone-releasing factor-(GRF) stimulated GH secretion. A phospholipase A2 inhibitor quinacrine (30 microM) increased cellular cAMP content while decreasing GH release. Indomethacin, which reduces cyclooxygenase activity, affected neither cAMP levels nor GRF-enhanced GH release; this drug (30-100 microM) did reduce basal GH release. The **lipoxygenase** inhibitors nordihydroguaiaretic acid and BW-755c both reduced basal and GRF-stimulated GH release in a concentration-dependent manner. Both agents had various effects on cAMP levels. These results suggest that phospholipid metabolism, through both the cyclooxygenase and **lipoxygenase** pathways, contributes to basal GH release, while the **lipoxygenase** route predominates in GRF-stimulated GH release in vitro. Interestingly, cAMP metabolism can be dissociated from GH release with some of these **probes**, indicating an action of phospholipid metabolites distal or lateral to the cAMP-generating system.

L4 ANSWER 52 OF 56 MEDLINE
Full Text
ACCESSION NUMBER: 83266701 MEDLINE
DOCUMENT NUMBER: 83266701 PubMed ID: 6409957
TITLE: A microassay of O2 concentrations based on oxygen-induced chemiluminescence in anaerobic lipoxygenase reactions.
AUTHOR: Laakso S; Huttunen T
SOURCE: JOURNAL OF BIOCHEMICAL AND BIOPHYSICAL METHODS, (1983 May) 7 (3) 211-6.
Journal code: H94; 7907378. ISSN: 0165-022X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198309
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19830920

AB The preparation of chemiluminescence **probes** for assaying O2 concentrations in microsamples is described. This probe is based on an anaerobic **lipoxygenase**-linoleate system continuously generating reactive intermediates which in a spontaneous reaction with added O2 yield an

excited species. The resulting chemiluminescence signals are highly reproducible upon repeated sample application and unaffected by even large variations in the contents of **lipoxygenase**-1 and linoleic acid. The linear assay range is between 0.25 and 25 nmol of O2. The assay system described is stable for 90 +/- 10 min, irrespective of the number of samples added, and the probe can be regenerated thereafter by adding linoleic acid.

L4 ANSWER 53 OF 56 MEDLINE
Full Text
ACCESSION NUMBER: 83067319 MEDLINE
DOCUMENT NUMBER: 83067319 PubMed ID: 6293050
TITLE: [Phagocytes and phagocytosis 100 years after Metchnikoff. A current picture of the neutrophil leukocyte]. Phagozyten und Phagozytose hundert Jahre nach Metschnikoff. Ein aktuelles Bild des neutrophilen Leukozyten.
AUTHOR: Baggiolini M
SOURCE: SCHWEIZERISCHE MEDIZINISCHE WOCHENSCHRIFT. JOURNAL SUISSE DE MEDECINE, (1982 Oct 9) 112 (41) 1403-11. Ref: 39
Journal code: UEI; 0404401. ISSN: 0036-7672.
PUB. COUNTRY: Switzerland
Biography
Historical
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198301
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19970203
Entered Medline: 19830107

AB The observation of the amoebocytes of primitive organisms led ELIAS METSCHNIKOFF in 1882 to the idea that blood phagocytes--neutrophilic leukocytes in particular--could constitute an anti-microbial defense system. This was the beginning of the phagocyte theory which METSCHNIKOFF developed over many years and which in essence is still valid. The author sets out to provide an updated view of the neutrophil. Circulating neutrophils are end-cells. They develop in the bone marrow by a relatively long maturation process during which the characteristic azurophil and specific granules are formed. The granules are stored organelles. The azurophil granules contain microbicidal enzymes, i.e. myeloperoxidase and lysozyme, together with a large number of acid hydrolases and neutral proteases. The specific granules contain lysozyme, a collagenase, lactoferrin and transcobalamines. By subcellular fractionation a third kind of storage organelle has recently been found which is characterized by its gelatinase content. Circulating neutrophils are activated on microbial invasion--first in the blood, by chemotactic factors formed at the site of infection, and subsequently by the **microbes** themselves which are phagocytosed by the immigrating neutrophils. Chemotactic factors lead to directed migration and induce the secretion of enzymes which presumably facilitate this process. Phagocytosis results in the mobilization of neutrophil products in large quantities. The contact between the cell and the microorganism activates in the neutrophil membrane an oxidase which produces superoxide, and a phospholipase which releases arachidonic acid. The latter is then oxidized by cyclooxygenase and **lipoxygenase**. There is also massive liberation of enzymes from all three storage compartments. The production of superoxide is the essential process for the killing of a large variety of microorganisms.

L4 ANSWER 54 OF 56 MEDLINE
Full Text
ACCESSION NUMBER: 82106763 MEDLINE
DOCUMENT NUMBER: 82106763 PubMed ID: 6275458
TITLE: Arachidonate metabolism in the mouse thyroid implication of the lipoxygenase pathway in thyrotropin action.
AUTHOR: Levasseur S; Sun F F; Friedman Y; Burke G
CONTRACT NUMBER: AM 1756107 (NIADDK)
SOURCE: PROSTAGLANDINS, (1981 Oct) 22 (4) 663-73.
Journal code: Q76; 0320271. ISSN: 0090-6980.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198203
ENTRY DATE: Entered STN: 19900317

Last Updated on STN: 19970203
Entered Medline: 19820313

AB The present study of compares the effects of various inhibitors of arachidonate metabolism on mouse thyroid cyclo-oxygenase and **lipoxygenase** activities and thyrotropin-augmented cyclic-AMP accumulation. Mouse thyroid homogenate converts [1-14C]- arachidonate to several products of the cyclo-oxygenase pathway as well as one major product of the **lipoxygenase** pathway, 12-L-hydroxyeicosatetraenoic acid (12-Hete). Prostaglandin (PG) formation in thyroid homogenates is inhibited by 1-10 microM indomethacin and etya. 12-HETE accumulation is reduced by 91%, 83% and 20% by 5 microM ETYA, 15-HETE, and indomethacin, respectively. Thyrotropin-stimulated cyclic-AMP accumulation, measured in whole thyroid **lobes** by radioimmunoassay, is reduced by 45% and 73% by 50 microM and 100 microM ETYA, respectively; indomethacin is without effect at these concentrations. 15-HETE reduces thyrotropin-augmented cyclic-AMP accumulation by 57% and 100 microM. In product inhibition studies, 10 microM 12-HETE reduced the formation of radiolabeled 12-HETE by 20%. 10 microM PGE2, PGF2 alpha or PGD2 had no effect on [1-14C]-PG formation. 12-HETE, however, reduced PG synthesis by 76% at 10 microM. This is the first report implicating the arachidonate **lipoxygenase** pathway in thyrotropin action at the level of cyclic-AMP regulation. Additionally, our finding that 12-HETE inhibits prostaglandin synthesis suggests that the cyclo-oxygenase and **lipoxygenase** pathways in the mouse thyroid may be highly integrated.

L4 ANSWER 55 OF 56 MEDLINE
Full Text
ACCESSION NUMBER: 81006966 MEDLINE
DOCUMENT NUMBER: 81006966 PubMed ID: 7410405
TITLE: Transformation of arachidonic acid into an iodolactone by the rat thyroid.
AUTHOR: Boeynaems J M; Hubbard W C
CONTRACT NUMBER: BRSG-RR-05424 (NCRR)
GM 15431 (NIGMS)
TW 02685 (FIC)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1980 Oct 10) 255 (19) 9001-4.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198011
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19801124

AB In the presence of iodide and hydrogen peroxide, lactoperoxidase, an enzyme model for thyroid peroxidase, catalyzed the conversion of arachidonic acid into several iodinated products. The major product was identified as 6-iodo-5-hydroxy-eicosatrienoic acid, delta-lactone (iodolactone), on the basis of 125I incorporation, mass spectrometry, proton magnetic resonance spectroscopy, and chemical modifications. Using this compound as a standard, two methods were developed to establish and quantitate the production of iodolactone by the rat thyroid in vitro: 125I labeling followed by reversed phase high pressure liquid chromatography and combined gas chromatography-mass spectrometry. Addition of iodide and arachidonic acid to rat thyroid **lobes** resulted in the formation and release of the iodolactone, which was inhibited by methimazole. These data suggest that peroxidases capable of oxidizing halides could provide a new pathway of arachidonic acid metabolism, besides cyclooxygenase and **lipoxygenases**.

L4 ANSWER 56 OF 56 MEDLINE
Full Text
ACCESSION NUMBER: 76227470 MEDLINE
DOCUMENT NUMBER: 76227470 PubMed ID: 820124
TITLE: [**Microbes** from soya beans. Inhibition of growth by **lipoxygenase** isoenzyme].
Mikroorganismen aus Sojabohnen. Hemmung des Wachstums durch ein Lipoxygenase-Isoenzym.
AUTHOR: Senser F; Grosch W
SOURCE: ZEITSCHRIFT FUR LEBENSMITTEL-UNTERSUCHUNG UND -FORSCHUNG, (1975 Oct 31) 159 (2) 103-6.
Journal code: YFA; 7509812. ISSN: 0044-3026.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197608
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19760823

AB Sixteen fungi and fife bacteria were isolated from soya beans and their species were determined. The microorganisms were cultivated on soya flour agar plates sterilized by heat. After addition of an enriched lipoxigenase preparation the growth was followed. The fungi but not the bacteria were all, to a varying degree, inhibited. Obviously the lipoxygenase peroxidizes the substrates occuring in the soya flour to compounds that inhibit the growth of the fungi.

=> s obes? or antiobes? or weight gain or weight loss or overweig?
66782 OBES?
167 ANTIOBES?
481023 WEIGHT
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494146 WEIGHT
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55665 GAIN
10367 GAINS
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23163 WEIGHT GAIN
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481023 WEIGHT
39371 WEIGHTS
494146 WEIGHT
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258169 LOSS
18443 LOSSES
269951 LOSS
(LOSS OR LOSSES)
22076 WEIGHT LOSS
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6323 OVERWEIG?
L5 104645 OBES? OR ANTIOBES? OR WEIGHT GAIN OR WEIGHT LOSS OR OVERWEIG?

=> s l5 ans l2
MISSING OPERATOR L5 ANS
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l5 and l2
L6 29 L5 AND L2

=> d ibib abs kwic 25-29

L6 ANSWER 25 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 91107479 MEDLINE
DOCUMENT NUMBER: 91107479 PubMed ID: 2125593
TITLE: Mechanism of phosgene-induced lung toxicity: role of arachidonate mediators.
AUTHOR: Guo Y L; Kennedy T P; Michael J R; Sciuto A M; Ghio A J; Adkinson N F Jr; Gurtner G H
CORPORATE SOURCE: Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland 21205.
CONTRACT NUMBER: 5K04-HL-02297 (NHLBI)
OH-02264 (NIOSH)
SOURCE: JOURNAL OF APPLIED PHYSIOLOGY, (1990 Nov) 69 (5) 1615-22.
Journal code: HEG; 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 19910329
Entered Medline: 19910228

AB We have previously shown that phosgene markedly increases lung weight

gain and pulmonary vascular permeability in rabbits. The current experiments were designed to determine whether cyclooxygenase- and lipoxygenase-derived mediators contribute to the phosgene induced lung injury. We exposed rabbits to phosgene (1,500 ppm/min), killed the animals 30 min later, and then perfused the lungs with a saline buffer for 90 min. Phosgene markedly increased lung weight gain, did not appear to increase the synthesis of cyclooxygenase metabolites, but increased 10-fold the synthesis of lipoxygenase products. Pre- or posttreatment with indomethacin decreased thromboxane and prostacyclin levels without affecting leukotriene synthesis and partially reduced the lung weight gain caused by phosgene. Methylprednisolone pretreatment completely blocked the increase in leukotriene synthesis and lung weight gain. Posttreatment with 5,8,11,14-eicosatetraynoic acid (ETYA), a nonmetabolized competitive inhibitor of arachidonic acid metabolism, or the leukotriene receptor blockers, FPL 55712 and LY 171883, also dramatically reduced the lung weight gain caused by phosgene. These results suggest that lipoxygenase products contribute to the phosgene-induced lung damage. Because phosgene exposure did not increase cyclooxygenase synthesis or pulmonary arterial pressure, we tested whether phosgene affects the lung's ability to generate or to react to thromboxane. Infusing arachidonic acid increased thromboxane synthesis to the same extent in phosgene-exposed lungs as in control lungs; however, phosgene exposure significantly reduced pulmonary vascular reactivity to thromboxane but not to angiotension II and KCl.

L6 ANSWER 26 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 90297478 MEDLINE
DOCUMENT NUMBER: 90297478 PubMed ID: 2193579
TITLE: Interleukin-1, anorexia, and dietary fatty acids.
AUTHOR: Dinarello C A; Endres S; Meydani S N; Meydani M; Hellerstein M K
CORPORATE SOURCE: Department of Medicine, Tufts University, Boston, Massachusetts.
CONTRACT NUMBER: AI15614 (NIAID)
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1990) 587 332-8. Ref: 11
Journal code: 5NM; 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19900907
Last Updated on STN: 19970203
Entered Medline: 19900801

AB IL-1 and other cytokines mediate several components of both acute and chronic pathological processes observed in patients with cancer and chronic infection. Cachexia ranks as one of the more prominent aspects of several diseases and the present studies demonstrate that recombinant forms of either IL-1 beta or IL-1 alpha reduce food intake in experimental animals. In meal-fed rats, a single injection of IL-1 induces a 40% reduction [table: see text] in food intake, whereas daily injections slow normal weight gain. The anorexic response to IL-1 is prevented by cyclooxygenase inhibitors, although this is unlikely due to a central nervous system effect. Reduced production of cyclooxygenase products such as PGE2 also occurs in rats fed supplemental N-3 fatty acids, and this was associated with a decreased anorexic response to IL-1. Therefore, one mechanism by which IL-1 induces anorexia appears to require cyclooxygenase metabolites, such as PGE2. N-3 fatty acid supplements also reduce the severity of host responses to inflammation and infection. Part of this is due to decreased cyclooxygenase products; however, part also may be due to reduced synthesis of IL-1. Blood leukocytes from human subjects taking oral N-3 supplements produce 60% less IL-1. The ability of N-3 fatty acids to reduce IL-1 synthesis appears to be via the lipoxygenase pathway. Therefore, N-3 fatty acids may be beneficial to patients with anorexia, since such supplements would decrease both the anorexic response to IL-1 via reduced cyclooxygenase metabolites and the production of IL-1, via altered lipoxygenase metabolites.

L6 ANSWER 27 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 90029141 MEDLINE

DOCUMENT NUMBER: 90029141 PubMed ID: 2508979
TITLE: Effect of canatoxin on the circulating levels of gonadotropins and prolactin in rats.
AUTHOR: Ribeiro-DaSilva G; Pires-Barbosa R; Carlini C R
CORPORATE SOURCE: Departamento de Farmacologia, Faculdade de Ciencias Medicas, Universidade Estadual de Campinas, SP, Brasil.
SOURCE: BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH, (1989) 22 (3) 387-95.
Journal code: BOF; 8112917. ISSN: 0100-879X.
PUB. COUNTRY: Brazil
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19900328
Entered Medline: 19891205

AB 1. The effects of canatoxin, the toxic principle from Canavalia ensiformis seeds which has **lipoxygenase**-activating properties, were evaluated in rats using radioimmunoassay techniques to measure plasma levels of prolactin (PRL), progesterone, follicle stimulating (FSH) and luteinizing (LH) hormones. 2. The chronic administration of canatoxin (50, 100 or 200 micrograms/kg daily for 12 days, ip) to female rats induced a sharp rise in plasma LH and FSH concentrations with no changes in progesterone level. A fall in circulating PRL was also observed. The frequency of proestrus and **weight gain** increased in rats treated with the highest dose of toxin used, but there was no alteration in weight of uterus or ovaries. 3. The increases in gonadotropin levels with canatoxin are consistent with the **lipoxygenase**-activating properties of the toxin, but do not explain why plasma PRL concentrations decreased in canatoxin-treated rats. 4. Since the animals in the control group had high PRL and low LH levels and since canatoxin increased LH and decreased PRL in the circulation, a possible stress-prevention effect is discussed for the toxin. 5. This study supports previous suggestions of central actions for canatoxin, and indicates the hypophysis and/or hypothalamus as one of the target sites for the toxin in the central nervous system.

L6 ANSWER 28 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 89168168 MEDLINE
DOCUMENT NUMBER: 89168168 PubMed ID: 2538226
TITLE: Effects of D,L-2-difluoromethylornithine and indomethacin on mammary tumor promotion in rats fed high n-3 and/or n-6 fat diets.
COMMENT: Erratum in: Cancer Res 1989 Sep 1;49(17):4946
AUTHOR: Abou-el-Ela S H; Prasse K W; Farrell R L; Carroll R W; Wade A E; Bunce O R
CORPORATE SOURCE: Department of Pharmacology and Toxicology, College of Pharmacy, University of Georgia, Athens 30602.
SOURCE: CANCER RESEARCH, (1989 Mar 15) 49 (6) 1434-40.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890426

AB Virgin female Sprague-Dawley rats (50 days of age) were administered a single intragastric 10-mg dose of 7,12-dimethylbenz(a)anthracene (DMBA). Twenty-one days later they were placed on diets containing either 20% corn oil (CO), 15% menhaden oil plus 5% corn oil (MO + CO), 20% CO plus 0.5% w/w of the irreversible ornithine decarboxylase inhibitor, D,L-2-difluoromethylornithine (CO + DFMO), 20% CO plus 0.004% w/w of the cyclooxygenase inhibitor indomethacin (CO + INDO), 20% CO + 0.004% INDO + 0.5% DFMO (CO + INDO + DFMO), or 15% MO + 5% CO + 0.5% DFMO (MO + CO + DFMO). The incidence of DMBA-induced mammary tumors was significantly reduced in rats fed diets containing DFMO but not in rats fed the diet containing indomethacin. Incidences of mammary tumors at 16 weeks post-DMBA were 86% in rats fed the CO diet, 83% in rats ingesting the diet containing CO + INDO, 28% in rats fed CO + DFMO, 32% in rats fed diet containing CO + INDO + DFMO, 59% in rats fed the MO + CO diet, and 24% in rats fed the MO + CO + DFMO diet. The average number of tumors and tumor burden per tumor-bearing rat were reduced and tumor latency was increased

in all rats fed diets containing DFMO. Body **weight gain**, but not food intake, of rats fed the 20% fat + 0.5% DFMO diets was significantly less than in rats fed the 20% fat diets. Prostaglandin E and leukotriene (LTB4) syntheses, ODC activity and mammary tumorigenesis were significantly inhibited by feeding the diet containing menhaden oil or by adding 0.5% DFMO to any of the high fat diets. Feeding a 20% CO diet containing 0.004% INDO significantly reduced prostaglandin synthesis and ODC activity and increased LTB4 synthesis of mammary tumors but did not inhibit mammary tumorigenesis. This study suggests that the 5-**lipoxygenase** product LTB4 may be involved in mammary tumor production. Whereas a decrease in LTB4 appears to be associated with a decrease in tumorigenesis, an increase (as seen in the indomethacin group) was not associated with any change in the tumorigenic response.

L6 ANSWER 29 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 89013081 MEDLINE
DOCUMENT NUMBER: 89013081 PubMed ID: 2459531
TITLE: Amiodarone causes acute oxidant lung injury in ventilated and perfused rabbit lungs.
AUTHOR: Kennedy T P; Gordon G B; Paky A; McShane A; Adkinson N F Jr; Peters S P; Friday K; Jackman W; Sciuto A M; Gurtner G H
CORPORATE SOURCE: Department of Medicine, University of Tennessee, Memphis.
SOURCE: JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, (1988 Jul) 12 (1) 23-36.
Journal code: K78; 7902492. ISSN: 0160-2446.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198811
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881108

AB Amiodarone (ADR), a new antiarrhythmic drug for life-threatening cardiac arrhythmias, causes pneumonitis or lung fibrosis in a sizeable minority of patients. The cause of lung damage is not known. We have shown that infusion of 10 mg amiodarone into the inflow circuit of ventilated and perfused rabbit lungs causes immediate increase in pulmonary artery pressure (mean +/- SEM) (from 13.6 +/- 1.2 to 40.6 +/- 9.5 mm Hg, p less than 0.01) and pulmonary edema with marked increase in the pulmonary generation of thromboxane and leukotrienes C4 and/or D4. Albumin (2 g%) in the perfusate prevents any increase in lung perfusion pressure or edema formation. When lung perfusion pressure increase is blocked with the combined cyclooxygenase and **lipoxygenase** inhibitor enolicam sodium (CG5391B, 35 microM in perfusate), significant lung edema still occurs after amiodarone, indicating that amiodarone causes increased alveolar-capillary membrane permeability. Addition of catalase (100 U/ml) or superoxide dismutase and catalase (100 U/ml each) to perfusate fails to protect from amiodarone lung injury. Immediate infusion of amiodarone (10 mg) into lungs ventilated with room air (ADR + RA) causes an increase in lung **weight gain** from baseline (delta W) of 5.7 +/- 1.5 g/min. Compared with ADR + RA, ventilation of lungs with 4% O2 (delta W = 0.7 +/- 0.3 g/min, p less than 0.05), pretreatment of rabbits for 3 days with butylated hydroxyanisole (BHA, 100 mg/kg/day i.p., delta W = 0.05 +/- 0.02 g/min, p less than 0.01), pretreatment of rabbits for 3 days with vitamin E (Vit E, 300 U/day orally, delta W = 0.6 +/- 0.2 g/min, p less than 0.05), or addition of N-acetylcysteine to the lung perfusate (NAC, 5 mM, delta W = 0.1 +/- 0.08 g/min, p less than 0.01) all protect from lung edema formation after amiodarone. Amiodarone (100 mg) also caused a marked increase in luminol-enhanced lung chemiluminescence, lung production of superoxide anion (O2-), and tissue levels of lung glutathione disulfide. These results suggest that amiodarone causes lung injury by an oxidant mechanism.

CT Check Tags: Animal; In Vitro; Male
*Amiodarone: TO, toxicity
*Antioxidants: PD, pharmacology
Arachidonate 5-Lipoxygenase: ME, metabolism
Arachidonic Acids: ME, metabolism
Glutathione: ME, metabolism
*Lung: DE, drug effects
Lung: ME, metabolism
Lung: PH,. . .

CN 0 (Antioxidants); 0 (Arachidonic Acids); EC 1.13.11.34 (Arachidonate

5-**Lipoxygenase**); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

=> d ibib abs kwic 20-24

L6 ANSWER 20 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 92354193 MEDLINE
DOCUMENT NUMBER: 92354193 PubMed ID: 1643751
TITLE: Enhanced metabolism of arachidonic acid by macrophages from nonobese diabetic (NOD) mice.
AUTHOR: Lety M A; Coulaud J; Bens M; Dardenne M; Homo-Delarche F
CORPORATE SOURCE: CNRS URA 1461, Hopital Necker, Paris, France.
SOURCE: CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1992 Sep) 64 (3) 188-96.
Journal code: DEA; 0356637. ISSN: 0090-1229.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19920925
Last Updated on STN: 19920925
Entered Medline: 19920908

AB The inbred nonobese diabetic (NOD) mouse spontaneously develops an autoimmune diabetes, which is now recognized as an experimental model for human type I insulin-dependent diabetes mellitus (IDDM). The autoimmune reaction, specifically directed against pancreatic beta cells (insulitis), involves both macrophages and T lymphocytes. The study of the production of cyclooxygenase and **lipoxygenase** derivatives of arachidonic acid metabolism shows that in some conditions, and in particular in the presence of zymosan A, macrophages from NOD mice produced significantly more 6-keto-prostaglandin F1 alpha (6-keto-PGF1 alpha) and leukotriene C4 (LTC4) than macrophages from age- and sex-matched C57BL/6 mice. Moreover, zymosan A-stimulated macrophages from NOD females produced significantly more LTC4 than did macrophages from NOD males. These results may be of interest, given the bidirectional relationship between the various cytokines involved in the destruction of beta cells of the islets of Langerhans and different eicosanoids.

CT . . .
Acid: ME, metabolism
Culture Media: PD, pharmacology
Leukotrienes: IM, immunology
Leukotrienes: ME, metabolism
*Macrophages: ME, metabolism
Mice
Mice, Inbred C57BL
***Mice, Obese: ME, metabolism**
Peritoneal Cavity: CY, cytology
Zymosan: PD, pharmacology

L6 ANSWER 21 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 92336524 MEDLINE
DOCUMENT NUMBER: 92336524 PubMed ID: 1632058
TITLE: Toxic peripheral neuropathy with demyelination in Sprague-Dawley rats given CGS 21595--a 5-**lipoxygenase** inhibitor.
AUTHOR: Gunson D E; Sahota P S; Iverson W O; Chau R Y; McCormick G M; Traina V M
CORPORATE SOURCE: Subdivision of Pathology, CIBA-GEIGY Corporation, Summit, NJ.
SOURCE: VETERINARY PATHOLOGY, (1992 Mar) 29 (2) 145-51.
Journal code: XBQ; 0312020. ISSN: 0300-9858.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920904
Last Updated on STN: 19920904
Entered Medline: 19920820

AB Male and female Sprague-Dawley rats were given CGS 21595, a pro-drug that is almost immediately metabolized to CGS 19213, a naphthoquinone that acts as a 5-**lipoxygenase** inhibitor. The compound was administered by gavage

to five groups of Sprague-Dawley rats (group Nos. 1, 5, n = 30; group Nos. 2-4, n = 20) at daily doses of 0, 50, 150, 500, or 1,000 mg/kg for 13 weeks. Rats in the higher dose groups had a reduced **weight gain**, but significant neurologic signs were not observed. A peripheral neuropathy consisting predominantly of myelin destruction in the spinal nerve roots and sciatic nerves in male rats treated with greater than or equal to 150 mg/kg CGS 21595 and in female rats treated with greater than or equal to 50 mg/kg CGS 21595 for 13 weeks. This lesion was not fully reversible after a recovery period of 4 weeks. Lesions consisted of ballooning of myelin sheaths, infiltration by macrophages, demyelination, and occasional areas of remyelination. Axons were generally preserved, and the brain and spinal cord were not affected. Male and female rats in all treatment groups had cytoplasmic hyaline droplets in the proximal renal tubules. This change was reversible after 4 weeks and was not associated with any other adverse effects on the kidney.

CT . . .
analogs & derivatives
1-Naphthylamine: CH, chemistry
1-Naphthylamine: TO, toxicity
Administration, Oral
Dose-Response Relationship, Drug
Kidney Tubules, Proximal: DE, drug effects
Lipoxygenase Inhibitors: AD, administration & dosage
Lipoxygenase Inhibitors: CH, chemistry
***Lipoxygenase Inhibitors: TO, toxicity**
Molecular Structure
Myelin Sheath: DE, drug effects
Prodrugs: AD, administration & dosage
Prodrugs: CH, chemistry
*Prodrugs: TO, toxicity
Rats
Rats, Inbred Strains
*Sciatic Nerve: DE, drug effects
*Spinal Nerve Roots: DE, drug effects
Weight Gain: DE, drug effects
CN 0 (**Lipoxygenase** Inhibitors); 0 (Prodrugs)

L6 ANSWER 22 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 92277229 MEDLINE
DOCUMENT NUMBER: 92277229 PubMed ID: 1317423
TITLE: Eicosanoids content in small intestinal mucosa of children with celiac disease.
COMMENT: Comment in: J Pediatr Gastroenterol Nutr. 1992 Nov;15(4):461
AUTHOR: Branski D; Hurvitz H; Halevi A; Klar A; Navon P; Weidenfeld J
CORPORATE SOURCE: Department of Pediatrics, Bikur Cholim General Hospital, Jerusalem, Israel.
SOURCE: JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION, (1992 Feb) 14 (2) 173-6.
Journal code: JL6; 8211545. ISSN: 0277-2116.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920701

AB Celiac disease (CD) is characterized by diarrhea, growth retardation, and **weight loss** in genetically susceptible subjects on a gluten-containing diet. The exact pathogenesis of CD is still obscure, but it is considered to be immunologically mediated. We have previously shown elevated prostaglandin E2 (PGE2) and thromboxane B2 (TxB2) content in small intestinal mucosa obtained from active celiac children. In the present study, we found significantly elevated PGE2, leukotriene B4 (LTB4), and leukotrienes C4, D4, and E4 (LTC4D4E4) content in small bowel mucosa from children suffering from CD on a gluten-containing diet in comparison to control subjects. PGE2 was 25,278 +/- 7,761 vs. 4,478 +/- 426 pg/mg of protein (mean +/- SEM), respectively. LTB4 was 8,807 +/- 3,706 vs. 403 +/- 63 pg/mg of protein (mean +/- SEM), respectively. LTC4D4E4 was 15,369 +/- 4,085 vs. 2,998 +/- 279 pg/mg of protein (mean +/- SEM), respectively. We conclude that the elevated content of arachidonic acid metabolic products via cyclooxygenase and **lipoxygenase** pathways may contribute to the

diarrhea and may be involved in the pathogenesis of mucosal injury.

L6 ANSWER 23 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 92230855 MEDLINE
DOCUMENT NUMBER: 92230855 PubMed ID: 1566864
TITLE: Role of eicosanoids in staphylococcal alpha-toxin-induced lung injury in the rat.
AUTHOR: Chang S W; Czartolomna J; Voelkel N F
CORPORATE SOURCE: Department of Medicine, University of Colorado Health Sciences Center, Denver 80262.
CONTRACT NUMBER: HL-01966 (NHLBI)
HL-07171 (NHLBI)
HL-14985 (NHLBI)
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1992 Apr) 262 (4 Pt 1) L502-10.
Journal code: 3U8; 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920607
Last Updated on STN: 19920607
Entered Medline: 19920521

AB We investigated the role of arachidonic acid-derived eicosanoids in staphylococcal alpha-toxin (alpha-T)-induced lung injury. Bolus injection of 200 and 500 micrograms alpha-T into isolated perfused rat lungs resulted in increased pulmonary perfusion pressure followed by lung **weight gain**. Inhibition of pressure change with papaverine (10(-4) M) failed to abolish lung edema. Furthermore, alpha-T increased the permeability-surface area product in papaverine-treated lungs and caused marked endothelial cell injury and interstitial edema as documented by electron microscopy. alpha-T dose dependently increased lung tissue thromboxane B2 (TxB2) levels and leukotriene C4 levels. In lungs given 0, 200, and 500 micrograms of alpha-T, TxB2 (in micrograms/g wet lung) values were 16.3 +/- 2.8, 25.0 +/- 3.0, and 54.2 +/- 6.2; and leukotriene C4 values were 4.6 +/- 1.1, 6.7 +/- 1.2, and 22.1 +/- 3.8, respectively. Inhibition of cyclooxygenase enzyme with indomethacin (10(-5) M) or **lipoxygenase** enzyme with 2(12-hydroxydodeca-5,10-dinyl)-3,5,6-trimethyl-1,4-benzoq uin one (AA861, 10(-5) M) attenuated the vasoconstriction and prevented lung edema due to low dose (200 micrograms) but not high dose (500 micrograms) alpha-T. The protective effect of these inhibitors on lung edema is in part due to decreases in alpha-T-stimulated venoconstriction because alpha-T-induced increase in lung microvascular pressure was attenuated by indomethacin and AA861 pretreatment. We conclude that both eicosanoid-dependent and eicosanoid-independent mechanisms contribute to alpha-T-induced lung edema in the rat.

L6 ANSWER 24 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 92225196 MEDLINE
DOCUMENT NUMBER: 92225196 PubMed ID: 1563537
TITLE: Effect of Tenidap, a novel anti-inflammatory compound on islet lymphocytic infiltration and diabetes incidence in the non **obese** diabetic (NOD) mouse.
AUTHOR: Beales P E; Williams A; Krug J; Signore A; Chianelli M; Andreani D; Pozzilli P
CORPORATE SOURCE: Department of Diabetes and Metabolism, St Bartholomew's Hospital, London, UK.
SOURCE: DIABETE ET METABOLISME, (1992 Jan-Feb) 18 (1) 48-53.
Journal code: E4J; 7604157. ISSN: 0338-1684.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920607
Last Updated on STN: 19920607
Entered Medline: 19920519

AB Tenidap, a novel compound inhibiting cyclooxygenase and **lipoxygenase**, also possessing an inhibitory effect on interleukin-1 secretion by in vitro activated macrophages, has been administered to the non **obese** diabetic (NOD) mouse to evaluate its action on the induction and progression of insulitis and the diabetes incidence. Animals were

allocated to three groups (group A: control group; group B: 12 mg/kg/day Tenidap; group C: 36 mg/kg/day Tenidap); female animals only were followed up to investigate the effect on diabetes incidence. The administration of Tenidap influenced the natural course of insulitis in male NOD mice; thus, at 60 and 100 days of age the mean percentage of infiltrated islets was significantly reduced compared to control animals (p less than 0.02). Moreover the severity of lymphocytic infiltration at 60 days of age was reduced in male mice of group B and C compared to control mice (p less than 0.004 and p less than 0.0001, respectively) whereas at 100 days of age this difference was not significant. However the progression towards severe insulitis in male animals receiving Tenidap was halted compared to control animals. Tenidap had also a significant dose dependent effect at 60 days on the severity of lymphocytic infiltration (group B vs. group C, p less than 0.01). By contrast, this agent had no effect on the degree of insulitis and diabetes incidence in female NOD mice. In both sexes at the end of follow-up a significant reduction in body weight was observed in animals of Group C compared to control animals (p less than 0.002).(ABSTRACT TRUNCATED AT 250 WORDS)

=> d ibib abs kwic 15-19

L6 ANSWER 15 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 94336704 MEDLINE
DOCUMENT NUMBER: 94336704 PubMed ID: 8058773
TITLE: Intrinsic 5-**lipoxygenase** activity is required for neutrophil responsivity.
AUTHOR: Guidot D M; Repine M J; Westcott J Y; Repine J E
CORPORATE SOURCE: Webb-Waring Institute for Biomedical Research, University of Colorado Health Sciences Center, Denver 80262.
CONTRACT NUMBER: K11-HL02690 (NHLBI)
P50-HL27353 (NHLBI)
RO 1-45582
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Aug 16) 91 (17) 8156-9.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940920
Last Updated on STN: 19970203
Entered Medline: 19940914

AB We found that intrinsic neutrophil 5-**lipoxygenase** activity was necessary for human neutrophil adherence and chemotaxis in vitro and human neutrophil-mediated acute edematous injury in isolated perfused rat lungs given interleukin 8 intratracheally. Treatment with either Zileuton (a specific reversible competitive inhibitor of 5-**lipoxygenase**) or MK886 (a specific irreversible inhibitor of the 5-**lipoxygenase** activator protein) prevented stimulated neutrophil adherence and chemotaxis (but not superoxide anion production) in vitro. Zileuton- or MK886-inhibited neutrophil chemotaxis was not restored by adding leukotriene B4 in vitro. Perfusion with neutrophils and either Zileuton or MK886, or with MK886-pretreated neutrophils (without adding MK886 to the perfusate), also prevented lung injury (reflected by lung **weight gain** and lung Ficoll retention) and perfusate leukotriene B4 increases in isolated rat lungs given interleukin 8 intratracheally. Again, adding leukotriene B4 to the perfusate did not damage interleukin 8-treated isolated lungs perfused with Zileuton-inhibited neutrophils. We conclude that intrinsic 5-**lipoxygenase** activity is required for neutrophil adherence and chemotaxis and neutrophil-mediated lung injury.

CT Check Tags: Animal; Human; In Vitro; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Arachidonate 5-Lipoxygenase: AI, antagonists & inhibitors
***Arachidonate 5-Lipoxygenase: BL, blood**
Cell Adhesion: DE, drug effects
*Chemotaxis, Leukocyte
Chemotaxis, Leukocyte: DE, drug effects
Cytochrome c: ME, metabolism
Dose-Response. . .

CN 0 (Indoles); 0 (Interleukin-8); 0 (Leukotrienes); 0 (Recombinant Proteins); EC 1.13.11.34 (Arachidonate 5-**Lipoxygenase**)

L6 ANSWER 16 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 94281949 MEDLINE
DOCUMENT NUMBER: 94281949 PubMed ID: 7764927
TITLE: Expression of desiccation-induced and **lipoxygenase** genes during the transition from the maturation to the germination phases in soybean somatic embryos.
AUTHOR: Liu W; Hildebrand D F; Moore P J; Collins G B
CORPORATE SOURCE: Department of Agronomy, University of Kentucky, Lexington 40546.
SOURCE: PLANTA, (1994) 194 (1) 69-76.
Journal code: BNG; 1250576. ISSN: 0032-0935.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: B
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19950809
Last Updated on STN: 19970203
Entered Medline: 19940727

AB Transitions between developmental programs during plant embryogenesis are usually characterized by differential gene expression. Soybean (Glycine max (L.) Merr.) somatic embryos from embryogenic suspension cultures germinate poorly on a germination medium even after being grown on medium containing abscisic acid until developmental changes are induced by desiccation. The objectives of this study were to investigate: (i) the relationship between water loss and germination of somatic embryos, (ii) changes in desiccation-induced polypeptides, and (iii) the expression of maturation- and germination-associated genes during the transition from maturation to germination of soybean somatic embryos. The results revealed that partial drying of somatic embryos at 76% relative humidity for 96 h resulted in more than 90% germination. Germination frequency was correlated with the percent fresh **weight loss** of the somatic embryos. Polypeptides induced by desiccation were classified into three groups based on the tissues in which they were expressed and the inducing agents to which they responded. Desiccation-induced polypeptides decreased or became undetectable upon inhibition. The expression of a maturation-associated gene, Mat1, was induced in both cotyledons and hypocotyl/radicle tissues of somatic embryos after 72 h desiccation. The transcript for this gene increased in concert with water loss from the embryos. During maturation of somatic embryos, the expression of embryonic **lipoxygenase** genes was turned on. Desiccation alone did not directly induce expression of germination-associated **lipoxygenase** genes SC514 and LOXB2 in somatic embryos.(ABSTRACT TRUNCATED AT 250 WORDS)

CT . . . Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Base Sequence
DNA Primers
*Desiccation
*Gene Expression
*Genes, Plant
Isoenzymes: GE, genetics
***Lipoxygenase: GE, genetics**
Molecular Sequence Data
Soybeans: EM, embryology
*Soybeans: GE, genetics
Tissue Culture
CN 0 (DNA Primers); 0 (Isoenzymes); EC 1.13.11.12 (**Lipoxygenase**)

L6 ANSWER 17 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 94258766 MEDLINE
DOCUMENT NUMBER: 94258766 PubMed ID: 8200079
TITLE: Inhibition of two-stage skin carcinogenesis as well as complete skin carcinogenesis by oral administration of TMK688, a potent **lipoxygenase** inhibitor.
AUTHOR: Jiang H; Yamamoto S; Kato R
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Keio University, Tokyo, Japan.
SOURCE: CARCINOGENESIS, (1994 May) 15 (5) 807-12.
Journal code: C9T; 8008055. ISSN: 0143-3334.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407

ENTRY DATE: Entered STN: 19940714
Last Updated on STN: 19970203
Entered Medline: 19940701

AB 1-([5'-(3''-methoxy-4''-ethoxycarbonyloxyphenyl)-2',4'-pentadienoyl]aminoethyl)-4-diphenylmethoxypiperidine (TMK688) is a potent and orally active 5-**lipoxygenase** inhibitor having anti-histamine activity in its moiety. Recently, we have found that TMK688 also inhibits epidermal cyclooxygenase activity with a potency similar to its inhibiting 5-**lipoxygenase**. Oral administration of 30 mg/kg TMK688, a dose which markedly inhibits tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA)-stimulated LTB4 formation in mouse skin, markedly inhibited both TPA-promoted and a non-TPA-type tumor promoter anthralin-promoted skin tumor formation in 7,12-dimethylbenz[a]anthracene (DMBA)-initiated CD-1 mice. The inhibitory effect of TMK688 was not due to any damage inflicted on the initiated cells but due to its antitumor-promoting activity. TMK688 not only inhibited two-stage skin carcinogenesis but also inhibited benzo[a]pyrene-caused complete skin carcinogenesis. Throughout the tumorigenesis experiment, the survival rate of animals was 100% and the TMK688-treated mice looked healthy. The body **weight gain** of TMK688-treated mice was not significantly different from that of non-treated mice. Both TMK688 and 1-([5'-(3''-methoxy-4''-hydroxyphenyl)-2',4'-pentadienoyl]amino eth yl]-4-diphenylmethoxypiperidine (TMK777), an active metabolite of TMK688 having more potent 5-**lipoxygenase** inhibitory activity and less potent cyclooxygenase inhibitory activity than TMK688, inhibited epidermal 8-**lipoxygenase** activity induced by a topical application of TPA to mouse skin. The 8-**lipoxygenase** inhibitory activity of TMK777 was approximately 5 times more potent than that of TMK688. Indomethacin, a typical cylcloxygenase inhibitor, in topical doses which almost completely inhibit epidermal PGE2 formation, failed to inhibit or only slightly inhibited DMBA-initiated and TPA-promoted skin tumor formation. These results suggest that the cyclooxygenase inhibitory effect of TMK688 is not essential for its anti-tumor promoting activity. Although at present a possible contribution of anti-histamine activity cannot be ruled out completely, the anti-tumor promoting action of TMK688 may most probably be related to its anti-**lipoxygenase** activity. TMK688 seems to be a promising agent for the prevention of skin carcinogenesis.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
9,10-Dimethyl-1,2-benzanthracene
Administration, Oral
Administration, Topical
*Anticarcinogenic Agents: TU, therapeutic use
Arachidonate Lipoxygenases: AI, antagonists & inhibitors
Benzo(a)pyrene
Indomethacin: PD, pharmacology
***Lipoxygenase Inhibitors: TU, therapeutic use**
Mice
Mice, Inbred Strains
Piperidines: ME, metabolism
*Piperidines: TU, therapeutic use
Skin: DE, drug effects
Skin:. . .

CN 0 (Anticarcinogenic Agents); 0 (**Lipoxygenase** Inhibitors); 0 (Piperidines); EC 1.13.11.- (Arachidonate **Lipoxygenases**); EC 1.13.11.40 (arachidonate 8-**lipoxygenase**)

L6 ANSWER 18 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 93270152 MEDLINE
DOCUMENT NUMBER: 93270152 PubMed ID: 8498596
TITLE: On the suppression of food intake in experimental models of colitis in the rat.
AUTHOR: McHugh K J; Weingarten H P; Keenan C; Wallace J L; Collins S M
CORPORATE SOURCE: Intestinal Disease Research Unit, McMaster University, Hamilton, Ontario, Canada.
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1993 May) 264 (5 Pt 2) R871-6.
Journal code: 3U8; 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930702
Last Updated on STN: 19970203

Entered Medline: 19930621

AB We measured daily food intake and body weight in rats before and after the induction of colitis by intrarectal administration of either 2,4,6-trinitrobenzenesulfonic acid in ethyl alcohol (TNBE) or 4% acetic acid (AA). Administration of TNBE or AA induced inflammation in the distal colon, which was reflected by a significant increase in myeloperoxidase (MPO) activity in the colon. On days 1, 2, and 3 after induction of colitis by TNBE, food intake fell by 80, 70, and 50%, respectively, compared with pretreatment values; food intake returned to normal by day 4. Body weight fell within 24 h after induction of colitis and remained 10% less than control for at least 5 days. Colitis induced by AA produced a similar pattern and degree of decreased food intake and **weight loss**. Treatment with the 5'-**lipoxygenase** inhibitor MK-886 significantly reduced concentrations of leukotriene B4 in the colon of TNBE-treated rats but did not affect food intake. In contrast, the cyclooxygenase inhibitor indomethacin decreased prostaglandin E2 concentrations in the colon but also attenuated the suppression of feeding by 52 and 64% on the first 2 days after induction of colitis by TNBE. These results identify a specific prostaglandin-mediated suppression of feeding in the rat with acute colitis induced by TNBE and illustrate the utility of this model for studying mechanisms underlying anorexia associated with inflammation of the gastrointestinal tract.

L6 ANSWER 19 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 93186584 MEDLINE
DOCUMENT NUMBER: 93186584 PubMed ID: 8444700
TITLE: Protection against platelet-activating factor-induced injury by interferon inducer in perfused rabbit lung.
AUTHOR: Huang Y C; Kennedy T P; Su Y F; Watkins W D; Whorton A R; Piantadosi C A
CORPORATE SOURCE: Department of Medicine, Duke University Medical Center, Durham, North Carolina 27710.
CONTRACT NUMBER: A249-906R4
SOURCE: JOURNAL OF APPLIED PHYSIOLOGY, (1993 Jan) 74 (1) 251-8. Journal code: HEG; 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930416
Last Updated on STN: 20000303
Entered Medline: 19930406

AB Platelet-activating factor (PAF) and the interferons (IFN) are released during sepsis and the adult respiratory distress syndrome. The proinflammatory nature of PAF and anti-inflammatory property of IFN led us to investigate interactions between these two mediators in an isolated perfused lung (IPL) preparation. In the IPL, mean pulmonary arterial pressure (Ppa), lung **weight gain**, and peak airway pressure (Paw) were monitored continuously for 1 h in six groups of rabbits: 1) control, 2) the IFN-alpha/beta inducer polyinosinic:cytidylic acid (polyI:C) alone, 3) PAF alone, 4) polyI:C + PAF, 5) indomethacin + PAF, and 6) AA861 (a 5-**lipoxygenase** inhibitor) + PAF. At the end of 1 h, microvascular pressure was determined by double-occlusion technique and partition of total pulmonary vascular resistance (RT) was calculated. Serial eicosanoid concentrations in the perfusate also were measured. PAF increased Ppa, Paw, lung **weight gain**, and RT. These changes were associated with increased thromboxane B2 and decreased leukotriene production. PolyI:C, which induced high levels of serum IFN in rabbits, blocked the PAF-induced increase in Ppa, Paw, lung **weight gain**, and RT, similar to indomethacin and AA861. PolyI:C suppressed PAF-stimulated release of thromboxane B2 and increased leukotriene levels in the perfusate. The PAF-induced lung responses also were attenuated by pretreatment with human recombinant IFN. These data indicate that polyI:C protects against PAF-induced responses in the rabbit IPL, most likely via its induction of IFN. This effect is related in part to inhibition of thromboxane A2 production stimulated by PAF and leukotrienes.

CT . . .
PC, prevention & control
Indicators and Reagents
Indomethacin: PD, pharmacology
*Interferon Inducers: PD, pharmacology
Interferon Type I, Recombinant: PD, pharmacology
Lipoxygenase Inhibitors: PD, pharmacology

Lung Diseases: CI, chemically induced
Lung Diseases: PP, physiopathology
*Lung Diseases: PC, prevention & control
Microcirculation:. . .
CN 0 (Arachidonic Acids); 0 (Benzoquinones); 0 (Indicators and Reagents); 0 (Interferon Inducers); 0 (Interferon Type I, Recombinant); 0 (**Lipoxygenase** Inhibitors); 0 (Platelet Activating Factor)

=> d ibib abs kwic 10-14

L6 ANSWER 10 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 1998081893 MEDLINE
DOCUMENT NUMBER: 98081893 PubMed ID: 9471228
TITLE: [Alterations of calcium, magnesium, and zinc in essential hypertension:their relation to the renin-angiotensin-aldosterone system].
Alteraciones del calcio, magnesio y zinc en hipertension es ncial: sus relaciones con el sistema renina-angiotensina aldosterona.
AUTHOR: Garcia Zozaya J L; Padilla Viloria M
CORPORATE SOURCE: Unidad de Hipertension Arterial, Hospital Enrique Tejera, Valencia, Estado Carabobo, Venezuela.
SOURCE: INVESTIGACION CLINICA, (1997 Nov) 38 Suppl 2 27-40.
Journal code: A18; 0421531. ISSN: 0535-5133.
PUB. COUNTRY: Venezuela
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980218

AB Based on our studies at the Hypertension research unit, we have found that the renin-angiotensin aldosterone. System (RAAS) undergoes several changes being the following the most relevant: Low plasma renin concentration (LPRC), while the plasma Aldosterone concentration is high (HPAC). At the same time we found calcium metabolism alterations: High urine calcium excretion, low serum ionic calcium and high PTH level. This alterations are more evident if the elder patient become hypertensive. We have found this changes in several groups in our community: black, ancient, **obese** and diabetic patients; who more often suffer hypertension and they must be followed up closely. In this group there are the sodium dependent hypertensive and they are the one who can get beneficial effects from the low salt diet and high calcium intake. When we studied the low plasma renin hypertensive we found the calcium changes mentioned before in ancient patient, as well as, high urine Zinc excretion. When we gave and oral calcium supplement to these patients, we saw that the calcium and Zinc alterations mentioned before were corrected. The high plasma renin concentration hypertensive patients showed low serum magnesium concentration and high urine magnesium excretion. A brief comment on the possible role of oxidative stress on essential hypertension is made.

CT . . .
ME, metabolism
Hypertension: DT, drug therapy
Hypertension: EP, epidemiology
Hypertension: ET, etiology
*Hypertension: ME, metabolism
Hypertension: PC, prevention & control
Lipoxygenase: ME, metabolism
*Magnesium: ME, metabolism
Middle Age
Models, Biological
Negroid Race: GE, genetics
Obesity: EP, epidemiology
Obesity: PP, physiopathology
Oxidative Stress
Parathyroid Hormones: ME, metabolism
Renin-Angiotensin System: DE, drug effects
*Renin-Angiotensin System: PH, physiology
Risk Factors
. . .
CN 0 (Antihypertensive Agents); 0 (Parathyroid Hormones); 0 (Sodium, Dietary); EC 1.13.11.12 (**Lipoxygenase**)

L6 ANSWER 11 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 97461835 MEDLINE
DOCUMENT NUMBER: 97461835 PubMed ID: 9316110
TITLE: Dietary fish oil or lofrin, a 5-**lipoxygenase** inhibitor, decrease the growth-suppressing effects of coccidiosis in broiler chicks.
AUTHOR: Korver D R; Wakenell P; Klasing K C
CORPORATE SOURCE: Department of Avian Sciences, School of Veterinary Medicine, University of California, Davis 95616, USA.
SOURCE: POULTRY SCIENCE, (1997 Oct) 76 (10) 1355-63.
Journal code: PG3; 0401150. ISSN: 0032-5791.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980129
Last Updated on STN: 20000303
Entered Medline: 19980113

AB Broiler chicks were fed a diet containing 4% of either corn oil or fish oil from 3 to 14 d of age. From Days 15 to 23, half of the chicks in each dietary treatment were fed Lofrin (an experimental 5-**lipoxygenase** inhibitor) at 33 micrograms/kg feed. The remaining chicks within each dietary treatment were the untreated controls. At 24 d of age, half of the chicks within each diet-Lofrin treatment group were each infected with 4.6 x 10(4) sporulated Eimeria tenella oocysts, resulting in a 2 x 2 x 2 factorial arrangement of treatments. Body **weight gain**, feed consumption, and feed conversion efficiency were determined throughout the study. At 27 d of age, blood, liver, and ceca were sampled. Plasma tumor necrosis factor and hemopexin, hepatic fatty acid composition, and cecal inflammatory cell infiltration were determined. Liver fatty acid composition tended to reflect that of the diet. Chicks fed fish oil had livers that were enriched in (n-3) polyunsaturated fatty acids (PUFA) at the expense of (n-6) PUFA. Chicks fed fish oil gained body weight more rapidly than those fed corn oil. Infection of chicks with Eimeria decreased body **weight gain** of chicks fed corn oil, but not of chicks fed fish oil. The addition of Lofrin to the corn oil diets abrogated the growth-suppressing effects of infection, although there was no Lofrin effect among chicks fed fish oil. There was a diet by Lofrin interaction in which Lofrin treatment of birds fed corn oil decreased feed consumption and increased feed conversion efficiency, but had no effect on chicks fed diets containing fish oil. Plasma hemopexin was greater, but tumor necrosis factor was lower, in chicks fed fish oil than in chicks fed corn oil. Eimeria infection significantly increased cecal inflammatory cell infiltration across all dietary treatments. There were no clear relationships between growth rate or efficiency and the severity of the inflammatory response to Eimeria infection, as indicated by hemopexin levels and cecal inflammatory scores. These results indicate that Lofrin or fish oil, both of which modify eicosanoid metabolism, attenuate the growth-depressing effects of an Eimeria tenella infection.

CT . . .
Hemopexin: ME, metabolism
Hydroxyurea: AD, administration & dosage
*Hydroxyurea: AA, analogs & derivatives
Hydroxyurea: PD, pharmacology
Leukotriene B4: ME, metabolism
Lipoxygenase Inhibitors: AD, administration & dosage
***Lipoxygenase Inhibitors: PD, pharmacology**
Liver: CH, chemistry
Poultry Diseases: PA, pathology
*Poultry Diseases: PP, physiopathology
Tumor Necrosis Factor: AN, analysis
Tumor. . .
CN 0 (Dietary Fats, Unsaturated); 0 (Fatty Acids); 0 (Fish Oils); 0 (**Lipoxygenase** Inhibitors); 0 (Tumor Necrosis Factor)

L6 ANSWER 12 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 97259592 MEDLINE
DOCUMENT NUMBER: 97259592 PubMed ID: 9105693
TITLE: Attenuation of diet-induced atherosclerosis in rabbits with a highly selective 15-**lipoxygenase** inhibitor lacking significant antioxidant properties.

AUTHOR: Sendobry S M; Cornicelli J A; Welch K; Bocan T; Tait B; Trivedi B K; Colbry N; Dyer R D; Feinmark S J; Daugherty A
CORPORATE SOURCE: Cardiovascular Division, Washington University School of Medicine, St. Louis, MO 63110, USA.
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1997 Apr) 120 (7) 1199-206.
Journal code: B00; 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970709
Last Updated on STN: 19970709
Entered Medline: 19970624

AB 1. 15-**Lipoxygenase** (15-LO) has been implicated in the pathogenesis of atherosclerosis because of its localization in lesions and the many biological activities exhibited by its products. To provide further evidence for a role of 15-LO, the effects of PD 146176 on the development of atherosclerosis in cholesterol-fed rabbits were assessed. This novel drug is a specific inhibitor of the enzyme in vitro and lacks significant non specific antioxidant properties. 2. PD 146176 inhibited rabbit reticulocyte 15-LO through a mixed noncompetitive mode with a Ki of 197 nM. The drug had minimal effects on either copper or 2,2'-azobis(2-amidinopropane)hydrochloride (ABAP) induced oxidation of LDL except at concentrations 2 orders higher than the Ki. 3. Control New Zealand rabbits were fed a high-fat diet containing 0.25% wt./wt. cholesterol; treated animals received inhibitor in this diet (175 mg kg-1, b.i.d.). Plasma concentrations of inhibitor were similar to the estimated Ki (197 nM). During the 12 week study, there were no significant differences in **weight gain** haematocrit, plasma total cholesterol concentrations, or distribution of lipoprotein cholesterol. 4. The drug plasma concentrations achieved in vivo did not inhibit low-density lipoprotein (LDL) oxidation in vitro. Furthermore, LDL isolated from PD 146176-treated animals was as susceptible as that from controls to oxidation ex vivo by either copper or ABAP. 5. PD 146176 was very effective in suppressing atherogenesis, especially in the aortic arch where lesion coverage diminished from 15 +/- 4 to 0% ($P < 0.02$); esterified cholesterol content was reduced from 2.1 +/- 0.7 to 0 micrograms mg-1 ($P < 0.02$) in this region. Immunostainable lipid-laden macrophages present in aortic intima of control animals were totally absent in the drug-treated group. 6. Results of these studies are consistent with a role for 15-LO in atherogenesis.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Antioxidants: PD, pharmacology
***Arachidonate 15-Lipoxygenase: AI, antagonists & inhibitors**
Arteriosclerosis: BL, blood
*Arteriosclerosis: DT, drug therapy
Arteriosclerosis: ET, etiology
*Diet
*Fluorenes: PD, pharmacology
Lipids: BL, blood
Lipoproteins: BL, blood
***Lipoxygenase Inhibitors: PD, pharmacology**
Rabbits
CN 0 (Antioxidants); 0 (Fluorenes); 0 (Lipids); 0 (Lipoproteins); 0 (**Lipoxygenase** Inhibitors); 0 (PD 146176); EC 1.13.11.33 (Arachidonate 15-**Lipoxygenase**)

L6 ANSWER 13 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 96403027 MEDLINE
DOCUMENT NUMBER: 96403027 PubMed ID: 8847296
TITLE: Intratracheal administration of DBcAMP attenuates edema formation in phosgene-induced acute lung injury.
AUTHOR: Sciuto A M; Strickland P T; Kennedy T P; Guo Y L; Gurtner G H
CORPORATE SOURCE: Physiology Branch, US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, Maryland 21010, USA.
SOURCE: JOURNAL OF APPLIED PHYSIOLOGY, (1996 Jan) 80 (1) 149-57.
Journal code: HEG; 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961024

AB Phosgene, a toxic gas widely used as an industrial chemical intermediate, is known to cause life-threatening latent noncardiogenic pulmonary edema. Mechanisms related to its toxicity appear to involve **lipoxygenase** mediators of arachidonic acid (AA) and can be inhibited by pretreatment with drugs that increase adenosine 3',5'-cyclic monophosphate (cAMP). In the present study, we used the isolated buffer-perfused rabbit lung model to investigate the mechanisms by which cAMP protects against phosgene-induced lung injury. Posttreatment with dibutyryl cAMP (DBcAMP) was given 60-85 min after exposure by an intravascular or intratracheal route. Lung **weight gain** (LWG) was measured continuously. AA metabolites leukotriene (LT) C4, LTD4, and LTE4 and 6-ketoprostaglandin F1 alpha were measured in the perfusate at 70, 90, 110, 130, and 150 min after exposure. Tissue malondialdehyde and reduced and oxidized glutathione were analyzed 150 min postexposure. Compared with measurements in the lungs of rabbits exposed to phosgene alone, posttreatment with DBcAMP significantly reduced LWG, pulmonary arterial pressure, and inhibited the release of LTC4, LTD4, and LTE4. Intratracheal administration of DBcAMP was more effective than intravascular administration in reducing LWG. Posttreatment also decreased MDA and protected against glutathione oxidation observed with phosgene exposure. We conclude that phosgene causes marked glutathione oxidation, lipid peroxidation, release of AA mediators, and increases LWG. Posttreatment with DBcAMP attenuates these effects, not only by previously described inhibition of pulmonary endothelial or epithelial cell contraction but also by inhibition of AA-mediator production and a novel antioxidant effect.

L6 ANSWER 14 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 95196689 MEDLINE
DOCUMENT NUMBER: 95196689 PubMed ID: 7889876
TITLE: Hypolipidemic, anti-**obesity**, anti-inflammatory, anti-osteoporotic, and anti-neoplastic properties of amine carboxyboranes.
AUTHOR: Hall I H; Chen S Y; Rajendran K G; Sood A; Spielvogel B F; Shih J
CORPORATE SOURCE: Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina Chapel Hill 27559-7360.
SOURCE: ENVIRONMENTAL HEALTH PERSPECTIVES, (1994 Nov) 102 Suppl 7 21-30. Ref: 30
Journal code: EI0; 0330411. ISSN: 0091-6765.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950427
Last Updated on STN: 19950427
Entered Medline: 19950420

AB The amine-carboxyborane derivatives were shown to be effective antineoplastic/cytotoxic agents with selective activity against single-cell and solid tumors derived from murine and human leukemias, lymphomas, sarcomas, and carcinomas. The agents inhibited DNA and RNA synthesis in preference to protein synthesis in L1210 lymphoid leukemia cells. Inosine-monophosphate dehydrogenase apparently is a target site of the compounds; similar effects on phosphoribosyl-pyrophosphate amido transferase, orotidine-monophosphate decarboxylase, and both nucleoside and nucleotide kinases were observed. Deoxyribonucleotide pool levels were reduced in the cells; DNA strand scission was observed with the agents. In rodents, the amine carboxyboranes were potent hypolipidemic agents, lowering both serum cholesterol and triglyceride concentrations, in addition to lowering cholesterol content of very low-density lipoprotein and low-density lipoprotein (LDL) and elevating high-density lipoprotein (HDL) cholesterol concentrations. De novo regulatory enzymes involved in lipid synthesis were also inhibited (e.g., hypocholesterolemic 3-hydroxy-3-methyl-Coenzyme A reductase, acyl-Coenzyme A cholesterol acyltransferase, and sn-glycerol-3-phosphate acyltransferase). Concurrently, the agents modulated LDL and HDL receptor binding,

internalization, and degradation, so that less cholesterol was delivered to the plaques and more broken down from esters and conducted to the liver for biliary excretion. Tissue lipids in the aorta wall of the rat were reduced and fewer atherosclerotic morphologic lesions were present in quail aortas after treatment with the agents. Cholesterol resorption from the rat intestine was reduced in the presence of drug. Genetic hyperlipidemic mice demonstrated the same types of reduction after treatment with the agents. The agents would effectively lower lipids in tissue based on the inhibition of regulatory enzymes in pigs. These findings should help improve domestic meat supplies from fowl and pigs. The amine-carboxyboranes were effective anti-inflammatory agents against septic shock, induced edema, pleurisy, and chronic arthritis at 2.5 to 8 mg/kg. Lysosomal and proteolytic enzyme activities were also inhibited. More significantly, the agents were dual inhibitors of prostaglandin cyclooxygenase and 5'-**lipoxygenase** activities. These compounds also affected cytokine release and white cell migration. Subsequent studies showed that the amine-carboxyboranes were potent anti-osteoporotic agents reducing calcium resorption as well as increasing calcium and proline incorporation into mouse pup calvaria and rat UMR-106 collagen.

CT . . .
Agents: TU, therapeutic use
*Boranes: TU, therapeutic use
*Hyperlipidemia: DT, drug therapy
*Inflammation: DT, drug therapy
*Neoplasms: DT, drug therapy
***Obesity: DT, drug therapy**

=> d ibib abs kwic 5-9

L6 ANSWER 5 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 2000127974 MEDLINE
DOCUMENT NUMBER: 20127974 PubMed ID: 10661911
TITLE: Benzofuranyl ureas with potent cardiovascular teratogenicity in rats.
AUTHOR: Solomon H M; Wier P J; Johnson C M; Posobiec L M; Rendemonti J E; Rumberger D F
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, King of Prussia, Pennsylvania 19406-0939, USA.
SOURCE: TERATOLOGY, (2000 Mar) 61 (3) 211-21.
Journal code: VM8; 0153257. ISSN: 0040-3709.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000412

AB Studies of embryo-fetal development in rats were conducted with two 5-**lipoxygenase** inhibitors. SB-202235 (1,000 mg/kg/day) or SB-210661 (50, 100, or 500 mg/kg/day) was administered orally by gavage to female rats on days 6-17 postcoitus (pc) or days 7-16 pc. SB-202235 (1,000 mg/kg/day) and SB-210661 (100 mg/kg/day) reduced maternal body **weight gain** for the treatment period by 16% and 21%, respectively, relative to controls. SB-202235 (1,000 mg/kg/day) or SB-210661 (50 or 100 mg/kg/day), did not affect numbers of resorptions, dead or live fetuses/litter, but 500 mg/kg/day of SB-210661 caused 100% embryo lethality. SB-202235 (1,000 mg/kg/day) and SB-210661 (50 and 100 mg/kg/day) reduced fetal body weight by 15-30% and produced extensive cardiovascular malformations, as well as diaphragmatic hernias. SB-210661 also caused thymic abnormalities and cryptorchidism. Cardiovascular defects included abnormalities in aorticopulmonary septation, the aortic arch, pulmonary trunk, and ventricular septal defects are discussed relative to comparable human syndromes of cardiovascular malformation.

CT . . . Animal; Female; Male
Abnormalities, Drug-Induced: EM, embryology
Aorta, Thoracic: AB, abnormalities
Aorta, Thoracic: DE, drug effects
Aorta, Thoracic: EM, embryology
***Arachidonate 5-Lipoxygenase: AI, antagonists & inhibitors**
*Benzofurans: TO, toxicity
*Cardiovascular System: DE, drug effects

Cardiovascular System: EM, embryology
Cardiovascular System: PA,. . .
CN 0 (Benzofurans); 0 (Enzyme Inhibitors); 0 (SB 202235); 0 (SB 210661); 0 (Teratogens); EC 1.13.11.34 (Arachidonate 5-**Lipoxygenase**)

L6 ANSWER 6 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 2000027706 MEDLINE
DOCUMENT NUMBER: 20027706 PubMed ID: 10556149
TITLE: Quinolines attenuate PAF-induced pulmonary pressor responses and edema formation.
AUTHOR: Falk S; Goggel R; Heydasch U; Brasch F; Muller K M; Wendel A; Uhlig S
CORPORATE SOURCE: Biochemical Pharmacology, University of Konstanz, Konstanz, Germany.
SOURCE: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, (1999 Nov) 160 (5 Pt 1) 1734-42.
Journal code: BZS; 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991221
AB In the present study we have investigated the mechanisms of pulmonary edema caused by platelet-activating factor (PAF) in isolated rat lungs as well as in mice in vivo. In blood-free perfused and ventilated rat lungs, PAF increased lung weight by 0.59 +/- 0.18 g. The cyclooxygenase inhibitor aspirin (500 microM) blocked this response by one-third, and the quinolines quinine (330 microM), quinidine (100 microM), and chloroquine (100 microM) by two-thirds. **Lipoxygenase** inhibition (10 microM AA861) alone or in combination with thromboxane receptor antagonism (10 microM SQ29548) had no effect on PAF-induced **weight gain**. In combination with aspirin, quinine or quinidine completely prevented PAF-induced **weight gain** and the concomitant increase of the capillary filtration coefficient (K(f,c)). Pretreatment with quinine in vivo prevented not only PAF-, but also endotoxin-induced edema formation as assessed by Evans Blue extravasation. In addition, in vivo quinine prevented the endotoxin-induced release of tumor neurosis factor (TNF). Furthermore, in perfused lungs quinine reduced the PAF-induced increases in airway and vascular resistance, as well as thromboxane release. These findings demonstrate the following anti-inflammatory properties of quinolines: reduction of thromboxane and TNF formation; reduction of PAF-induced vasoconstriction and bronchoconstriction; and attenuation of PAF- and lipopolysaccharide (LPS)-induced edema formation. We conclude that the PAF- induced edema consists of two separate mechanisms, one dependent on an unknown cyclooxygenase metabolite, the other one sensitive to quinolines.
CT . . .
PD, pharmacology
Benzoquinones: PD, pharmacology
Capillary Permeability
Chloroquine: PD, pharmacology
Cyclooxygenase Inhibitors: PD, pharmacology
Hydrazines: PD, pharmacology
Interleukin-6: ME, metabolism
Lipoxygenase Inhibitors: PD, pharmacology
Lung: BS, blood supply
*Lung: ME, metabolism
Mice
Mice, Inbred BALB C
*Platelet Activating Factor: PH,. . .
CN 0 (Benzoquinones); 0 (Cyclooxygenase Inhibitors); 0 (Hydrazines); 0 (Interleukin-6); 0 (**Lipoxygenase** Inhibitors); 0 (Platelet Activating Factor); 0 (Quinolines); 0 (Receptors, Thromboxane); 0 (Tumor Necrosis Factor)

L6 ANSWER 7 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 1999128377 MEDLINE
DOCUMENT NUMBER: 99128377 PubMed ID: 9927708
TITLE: Antisense-mediated depletion of a potato **lipoxygenase** reduces wound induction of proteinase inhibitors and

increases **weight gain** of insect pests.

AUTHOR: Royo J; Leon J; Vancanneyt G; Albar J P; Rosahl S; Ortego F; Castanera P; Sanchez-Serrano J J
CORPORATE SOURCE: Departamento, Centro Nacional de Biotecnologia, Consejo Superior de Investigaciones Cientificas, Campus Cantoblanco Universidad Autonotia de Tiadrid, 28049 Madrid, Spain.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Feb 2) 96 (3) 1146-51.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990305

AB De novo jasmonic acid (JA) synthesis is required for wound-induced expression of proteinase inhibitors and other defense genes in potato and tomato. The first step in JA biosynthesis involves **lipoxygenase** (LOX) introducing molecular oxygen at the C-13 position of linolenic acid. We previously have shown that, in potato, at least two gene families code for 13-LOX proteins. We have now produced transgenic potato plants devoid of one specific 13-LOX isoform (LOX-H3) through antisense-mediated depletion of its mRNA. LOX-H3 depletion largely abolishes accumulation of proteinase inhibitors on wounding, indicating that this specific LOX plays an instrumental role in the regulation of wound-induced gene expression. As a consequence, **weight gain** of Colorado potato beetles fed on antisense plants is significantly larger than those fed on wild-type plants. The poorer performance of LOX-H3-deficient plants toward herbivory is more evident with a polyphagous insect; larvae of beet armyworm reared on the antisense lines have up to 57% higher weight than those fed on nontransformed plants. LOX-H3 thus appears to regulate gene activation in response to pest attack, and this inducible response is likely to be a major determinant for reducing performance of nonspecialized herbivores. However, the regulatory role of LOX-H3 is not caused by its involvement in the wound-induced increase of JA, as wild-type and LOX-H3 deficient plants have similar jasmonate levels after wounding. LOX-H3-deficient plants have higher tuber yields. The apparent effect of suppressing the inducible defensive response on plant vigor suggests that it may pose a penalty in plant fitness under nonstress situations.

CT . . .
genetics
Amino Acid Sequence
Antibodies
*Beetles: GD, growth & development
*Cyclopentanes: ME, metabolism
*DNA, Antisense
*Gene Expression Regulation, Plant
Larva
Lipoxygenase: AN, analysis
Lipoxygenase: CH, chemistry
***Lipoxygenase: GE, genetics**
Lipoxygenase: ME, metabolism
Molecular Sequence Data
Peptide Fragments: CH, chemistry
Peptide Fragments: IM, immunology
Plant Leaves
Plants, Transgenic
Potatoes: GE, genetics
Potatoes: PS, parasitology
*Potatoes: PH, physiology
*Protease Inhibitors: ME, metabolism
RNA, Messenger: GE, genetics
Transcription, Genetic
Weight Gain
Wounds and Injuries
CN 0 (Antibodies); 0 (Cyclopentanes); 0 (DNA, Antisense); 0 (Peptide Fragments); 0 (Protease Inhibitors); 0 (RNA, Messenger); EC 1.13.11.- (13-**lipoxygenase**); EC 1.13.11.12 (**Lipoxygenase**)

L6 ANSWER 8 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 1998371667 MEDLINE
DOCUMENT NUMBER: 98371667 PubMed ID: 9706378

TITLE: Anti-inflammatory and immunomodulating properties of grape melanin. Inhibitory effects on paw edema and adjuvant induced disease.
AUTHOR: Avramidis N; Kourounakis A; Hadjipetrou L; Senchuk V
CORPORATE SOURCE: Department of Genetics, Development and Molecular Biology, School of Biology, Faculty of Sciences, Aristoteles University of Thessaloniki, Greece.
SOURCE: ARZNEIMITTEL-FORSCHUNG, (1998 Jul) 48 (7) 764-71.
Journal code: 91U; 0372660. ISSN: 0004-4172.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980916

AB Natural or synthetic melanin (CAS 8049-97-6) is a high molecular weight heteropolymer, product of the enzyme tyrosinase, found to possess radical scavenging and antioxidant functions. It was of interest, therefore, to study in detail the possible anti-inflammatory and/or immunosuppressive properties of a melanin isolated from grapes. The inhibitory effect of melanin on carrageenin-induced edema, as well as on edemas produced by other phlogistics, was remarkable suggesting that melanin interferes with the prostaglandin as well as the leukotriene and/or complement system mediated inflammation. Grape melanin showed potent inhibitory effect on adjuvant induced disease (AID) in rat, suppressing significantly the primary inflammation and almost totally the secondary lesions of arthritis. Melanin under the present experimental conditions not only strongly inhibited the in vitro lipid peroxidation of rat liver microsomal membranes, but furthermore protected the in vivo hepatic peroxidation occurring in AID rats, demonstrating its antioxidant and cytoprotective properties. The serum proinflammatory cytokines IL-1, IL-6 and TNF-a and the serum globulin fraction were elevated in AID rats, parameters which were more or less normalised by melanin treatment in contrast to the reduced serum levels of IL-2 which were not affected. Similarly to other **lipoxygenase** inhibitors and hydroxyl radical scavenger NSAIDs, melanin treatment did not affect IL-1 neither increased the splenic mitogenic responses, unlike the classical cyclooxygenase inhibitory NSAIDs. The subpopulation Th1 (T4+ or T8+) of lymphocytes is mainly responsible for cellular immune responses and thus their possible inhibition by melanin could lead to suppression of the development of AID, a model for cell-mediated immunity. The effect of melanin on T-cells is exhibited by the reduced spleen mitogenic responses to a T-cell mitogen and the reduced serum levels of IL-2 of treated rats. In conclusion, grape melanin is an interesting anti-inflammatory and immunomodulating natural product which appears to have multiple cellular targets within the reticuloendothelial and immune system.

CT . . .
pharmacology
Organ Weight: DE, drug effects
Phagocytosis: DE, drug effects
Rats
Rats, Inbred F344
*Rosales: CH, chemistry
Spleen: CY, cytology
Weight Gain: DE, drug effects

L6 ANSWER 9 OF 29 MEDLINE
Full Text
ACCESSION NUMBER: 1998160195 MEDLINE
DOCUMENT NUMBER: 98160195 PubMed ID: 9500559
TITLE: Decreased activity of arachidonate 12-**lipoxygenase** in platelets of Japanese patients with non-insulin-dependent diabetes mellitus.
AUTHOR: Tohjima T; Honda N; Mochizuki K; Kinoshita J; Watanabe K; Arisaka T; Kawamori R; Nakamura M; Kurahashi Y; Yoshimoto T; Yamamoto S
CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology, Juntendo University School of Medicine, Tokyo, Japan.
SOURCE: METABOLISM: CLINICAL AND EXPERIMENTAL, (1998 Mar) 47 (3) 257-63.
Journal code: MUM; 0375267. ISSN: 0026-0495.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980326
Last Updated on STN: 19980326
Entered Medline: 19980319

AB To study the metabolism of the platelet 12-**lipoxygenase** pathway in diabetes, we evaluated the correlation between the activity and amount of arachidonate 12-**lipoxygenase** in the platelets of patients with non-insulin-dependent-diabetes mellitus (NIDDM). There were four parts in this investigation: (1) examination of abnormalities in platelet 12-**lipoxygenase** in patients with NIDDM recruited from the Hospital of Juntendo University School of Medicine; (2) comparison of 12-**lipoxygenase** in the platelets of non-**obese** NIDDM patients without angiopathy versus normal subjects matched for age, sex, and body mass index (BMI); (3) evaluation of gender differences; and (4) assessment of the potential influence of glycemic control. The activity of 12-**lipoxygenase** was assayed by incubation of [1-14C]arachidonic acid with the platelet cytosol. The reaction mixture was extracted and separated by thin-layer chromatography, and the radioactive end products were detected. The activity of 12-**lipoxygenase** in the platelets of patients with NIDDM was significantly less than in normal subjects ($P < .003$), whereas the amount of 12-**lipoxygenase** protein did not differ between the two groups. Thus, the specific activity of 12-**lipoxygenase** in diabetic patients was significantly less than that of normal subjects ($P < .001$). The enzyme activity and the specific enzyme activity of 12-**lipoxygenase** in non-**obese** NIDDM patients without angiopathy were significantly lower than the values in normal subjects matched for gender, age, and BMI ($P < .006$ and $P < .0007$, respectively). No significant difference in the activity or amount of platelet 12-**lipoxygenase** was observed between males and females matched for age, BMI, and disease. In addition, no relationship was observed between 12-**lipoxygenase** activity and blood glucose levels measured at the time of specimen collection. However, slight negative correlations were noted between 12-**lipoxygenase** activity and 1,5-anhydroglucitol, hemoglobin A1c (HbA1c), and fructosamine ($r = .369$, $-.354$, and $-.279$, respectively). When recombinant 12-**lipoxygenase** was incubated with varying concentrations of glucose or fructose, enzyme inactivation was related to the length of incubation, and was unaffected by glucose or fructose. These observations suggest that the activity of 12-**lipoxygenase** in the platelets of patients with NIDDM is decreased by prolonged hyperglycemia. The mechanism involved requires further investigation.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
***Arachidonate 12-Lipoxygenase: BL, blood**
Arachidonic Acid: ME, metabolism
Blood Glucose: ME, metabolism
*Blood Platelets: EN, enzymology
Body Mass Index
Cytosol: EN,. . .

CN 0 (Blood Glucose); 0 (Hemoglobin A, Glycosylated); EC 1.13.11.31 (Arachidonate 12-**Lipoxygenase**)

=> d his

(FILE 'HOME' ENTERED AT 22:26:50 ON 13 MAY 2002)

FILE 'MEDLINE' ENTERED AT 22:27:25 ON 13 MAY 2002
L1 194642 S ?OBES? OR WEIGHT GAIN OR WEIGHT LOSS OR OVERWEIGH?
L2 10042 S LIPOXYGENASE
L3 87 S L1 AND L2
L4 56 S L1 (S) L2
L5 104645 S OBES? OR ANTIOBES? OR WEIGHT GAIN OR WEIGHT LOSS OR OVERWEIG?
L6 29 S L5 AND L2

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=> s l2
L7       29691 L2

=> s l5
L8      229462 L5

=> s l7 and l8
L9         258 L7 AND L8

=> s l7 (S) l8
L10         45 L7 (S) L8

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11          40 DUP REM L10 (5 DUPLICATES REMOVED)

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L11  ANSWER 35 OF 40  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
ACCESSION NUMBER:   1992:309822  BIOSIS
DOCUMENT NUMBER:    BA94:22972
TITLE:              ROLE OF EICOSANOIDS IN STAPHYLOCOCCAL ALPHA TOXIN-INDUCED
                    LUNG INJURY IN THE RAT.
AUTHOR(S):          CHANG S-W; CZARTOLOMNA J; VOELKEL N F
CORPORATE SOURCE:   PULMONARY SECTION, DEP. MED., NORTHWESTERN UNIV. MED. SCH.,
                    250 E. SUPERIOR, RM. 456, CHICAGO, ILLINOIS 60611, USA.
SOURCE:             AM J PHYSIOL, (1992) 262 (4 PART 1), L502-L510.
                    CODEN: AJPHAP. ISSN: 0002-9513.
FILE SEGMENT:       BA; OLD
LANGUAGE:           English
AB   We investigated the role of arachidonic acid-derived eicosanoids in
     staphylococcal α-toxin (α-T)-induced lung injury. Bolus
     injection of 200 and 500 μg α-T into isolated perfused rat lungs
     resulted in increased pulmonary perfusion pressure followed by lung
     weight gain. Inhibition of pressure change with papaverine (10-4 M)
     failed to abolish lung edema. Furthermore, α-T increased the
     permeability-surface area product in papaverine-treated lungs and caused
     marked endothelial cell injury and interstitial edema as documented by
     electron microscopy. α-T dose dependently increased lung tissue
     thromboxane B2 (TxB2) levels and leukotriene C4 levels. In lungs given 0,
     200, and 500 μg of α-T, TxB2 (in μg/g wet lung) values were
     16.3 ± 2.8, 25.0 ± 3.0, and 54.2 ± 6.2; and leukotriene C4 values
     were 4.6 ± 1.1, 6.7 ± 1.2, and 22.1 ± 3.8, respectively.
     Inhibition of cyclooxygenase enzyme with indomethacin (10-5 M) or
     lipoxygenase enzyme with 2(12-hydroxydodeca-5,10-dinyl)-3,5,6-trimethyl-
     1,4-benzoquinone (AA861, 10-5 M) attenuated the vasoconstriction and
     prevented lung edema due to low dose (200 μg) but not high dose (500
     μg) α-T. The protective effect of these inhibitors on lung edema
     is in part due to decreases in α-T-stimulated venoconstriction
     because α-T-induced increase in lung microvascular pressure was
     attenuate by indomethacin and AA861 pretreatment. We conclude that both
     eicosanoid-dependent and eicosanoid-independent mechanisms contribute to
     α-T-induced lung edema in the rat.

L11  ANSWER 36 OF 40  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
ACCESSION NUMBER:   1992:255807  BIOSIS
DOCUMENT NUMBER:    BA93:132132
TITLE:              EICOSANOIDS CONTENT IN SMALL INTESTINAL MUCOSA OF CHILDREN
                    WITH CELIAC DISEASE.
AUTHOR(S):          BRANSKI D; HURVITZ H; HALEVI A; KLAR A; NAVON P; WEIDENFELD
                    J
CORPORATE SOURCE:   DEP. PEDIATRICS, SHAARE ZEDEK MED. CENT., P.O. BOX 3235,
```

JERUSALEM 91031, ISRAEL.
SOURCE: J PEDIATR GASTROENTEROL NUTR, (1992) 14 (2), 173-176.
CODEN: JPGND6. ISSN: 0277-2116.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Celiac disease (CD) is characterized by diarrhea, growth retardation, and **weight loss** in genetically susceptible subjects on a gluten-containing diet. The exact pathogenesis of CD is still obscure, but it is considered to be immunologically mediated. We have previously shown elevated prostaglandin E2 (PGE2) and thromboxane B2 (TxB2) content in samll intestinal mulcosa obtained from active celiac children. In the present study, we found significantly elevated PGE2, leukotriene B4 (LTB4), and leukotrienes C4,D4, and E4 (LTC4D4E4) content in small bowel mucosa from children suffering from CD on a gluten-containing diet in comparison to control subjects. PGE2 was 25,278 ± 7,761 vs. 4,478 ± 426 pg/mg of protein (mean ± SEM), respectively. LTB4 was 8,807 ± 3,706 vs. 403 ± 63 pg/mg of protein (mean ± SEM), respectively. LTC4D4E4 was 15,369 ± 4,085 vs. 2,998 ± 279 pg/mg of protein (mean ± SEM), respectively. We conclude that the elevated content of arachidonic acid metabolic products va cyclooxygenase and **lipoxygenase** pathways may contribute to the diarrhea and may be involved in the pathogenesis of muscosal injury.

IT Miscellaneous Descriptors
ELEVATED PROSTAGLANDIN E2 ELEVATED THROMBOXANE B2 LEUKOTRIENE B4 DIARRHEA GROWTH RETARDATION **WEIGHT LOSS** GLUTEN-SENSITIVE ENTEROPATHY ELEVATED ARACHIDONIC ACID METABOLIC PRODUCTS CONTENT CYCLOOXYGENASE PATHWAY **LIPOXYGENASE** PATHWAY

L11 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2002 ACS
Full Text
ACCESSION NUMBER: 1993:420275 CAPLUS
DOCUMENT NUMBER: 119:20275
TITLE: Effect of Tenidap, a novel anti-inflammatory compound on islet lymphocytic infiltration and diabetes incidence in the non obese diabetic (NOD) mouse
AUTHOR(S): Beales, P. E.; Williams, A.; Krug, J.; Signore, A.; Chianelli, M.; Andreani, D.; Pozzilli, P.
CORPORATE SOURCE: Dep. Diabetes Metab., St Bartholomew's Hosp., London, EC1A 7BE, UK
SOURCE: Diabete Metab. (1992), 18(1), 48-53
CODEN: DIMEDU; ISSN: 0338-1684
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tenidap, a novel compd. inhibiting cyclooxygenase and **lipoxygenase**, also possessing an inhibitory effect on interleukin-1 secretion by in vitro activated macrophages, has been administered to the non **obese** diabetic (NOD) mouse to evaluate its action on the induction and progression of insulitis and the diabetes incidence. Animals were allocated to three groups (group A: control group; group B: 12 mg/kg/day Tenidap; group C: 36 mg/kg/day Tenidap); female animals only were followed up to investigate the effect on diabetes incidence. The administration of Tenidap influenced the natural course of insulitis in male NOD mice; thus, at 60 and 100 days of age the mean percentage of infiltrated islets was significantly reduced compared to control animals ($p < 0.02$). Moreover the severity of lymphocytic infiltration at 60 days of age was reduced in male mice of group B and C compared to control mice ($p < 0.004$ and $p < 0.0001$, resp.) whereas at 100 days of age this difference was not significant. However the progression towards severe insulitis in male animals receiving Tenidap was halted compared to control animals. Tenidap had also a significant dose dependent effect at 60 days on the severity of lymphocytic infiltration (group B vs. group C, $p < 0.01$). By contrast, this agent had no effect on the degree of insulitis and diabetes incidence in female NOD mice. In both sexes at the end of follow-up a significant redn. in body wt. was obsd. in animals of Group C compared to control animals ($p < 0.002$). We conclude that Tenidap, at pharmacol. doses, reduces the lymphocytic infiltration in the pancreas of male NOD mice but does not protect female mice from developing the disease suggesting the importance of the sex hormone pattern in the pathogenesis of diabetes in this animal model.

L11 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
Full Text
ACCESSION NUMBER: 1991:158673 CAPLUS
DOCUMENT NUMBER: 114:158673
TITLE: Mechanism of phosgene-induced lung toxicity: role of

arachidonate mediators
AUTHOR(S): Guo, Yue Liang; Kennedy, Thomas P.; Michael, John R.; Sciuto, A. Mario; Ghio, Andrew J.; Adkinson, N. Franklin, Jr.; Gurtner, Gail H.
CORPORATE SOURCE: Dep. Med., Johns Hopkins Med. Inst., Baltimore, MD, 21205, USA
SOURCE: J. Appl. Physiol. (1990), 69(5), 1615-22
CODEN: JAPHEV; ISSN: 8750-7587
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phosgene markedly increases lung wt. gain and pulmonary vascular permeability in rabbits. The current expts. were designed to det. whether cyclooxygenase- and lipoxygenase-derived mediators contribute to the phosgene-induced lung injury. Rabbits were exposed to phosgene (1500 ppm/min), the animals killed 30 min later, and then the lungs perfused with a saline buffer for 90 min. Phosgene markedly increased lung wt. gain, did not appear to increase the synthesis of cyclooxygenase metabolites, but increased 10-fold the synthesis of lipoxygenase products. Pre- or posttreatment with indomethacin decreased thromboxane and prostacyclin levels without affecting leukotriene synthesis and partially reduced the lung wt. gain caused by phosgene. Methylprednisolone pretreatment completely blocked the increase in leukotriene synthesis and lung wt. gain. Posttreatment with 5,8,11,14-eicosatetraynoic acid, a nonmetabolized competitive inhibitor of arachidonic acid metab., or the leukotriene receptor blockers, FPL 55712 and LY 171883, also dramatically reduced the lung wt. gain caused by phosgene. These results suggest that lipoxygenase products contribute to the phosgene-induced lung damage. Because phosgene exposure did not increase cyclooxygenase synthesis or pulmonary arterial pressure, the authors tested whether phosgene affects the lung's ability to generate or to react to thromboxane. Infusing arachidonic acid increased thromboxane synthesis to the same extent in phosgene-exposed lungs as in control lungs; however, phosgene exposure significantly reduced pulmonary vascular reactivity to thromboxane but not to angiotensin II and KCl.

L11 ANSWER 39 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
ACCESSION NUMBER: 1989:205184 BIOSIS
DOCUMENT NUMBER: BA87:106088
TITLE: EFFECTS OF D L-2 DIFLUOROMETHYLORNITHINE AND INDOMETHACIN ON MAMMARY TUMOR PROMOTION IN RATS FED HIGH N-3 AND-OR N-6 FAT DIETS.
AUTHOR(S): ABOU-EL-ELA S H; PRASSE K W; FARRELL R L; CARROLL R W; WADE A E; BUNCE O R
CORPORATE SOURCE: DEP. PHARMACOL. TOXICOL., COLL. PHARM., UNIV. GEORGIA, ATHENS, GA. 30602.
SOURCE: CANCER RES, (1989) 49 (6), 1434-1440.
CODEN: CNREA8. ISSN: 0008-5472.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Virgin female Sprague-Dawley rats (50 days of age) were administered a single intragastric 10-mg dose of 7,12-dimethylbenz(a)anthracene (DMBA). Twenty-one days later they were placed on diets containing either 20% corn oil (CO), 15% menhaden oil plus 5% corn oil (MO + CO), 20% CO plus 0.5% w/w of the irreversible ornithine decarboxylase inhibitor, D,L-2-difluoromethylornithine (CO + DFMO), 20% CO plus 0.004% w/w of the cyclooxygenase inhibitor indomethacin (CO + INDO), 20% CO + 0.004% INDO + 0.5% DFMO (CO + INDO + DFMO), or 15% MO + 5% CO + 0.5% DFMO (MO + CO + DFMO). The incidence of DMBA-induced mammary tumors was significantly reduced in rats fed diets containing DFMO but not in rats fed the diet containing indomethacin. Incidences of mammary tumors at 16 weeks post-DMBA were 86% in rats fed the CO diet, 83% in rats ingesting the diet containing CO + INDO, 28% in rats fed CO + DFMO, 32% in rats fed diet containing CO + INDO + DFMO, 59% in rats fed the MO + CO diet, and 24% in rats fed the MO + CO + DFMO diet. The average number of tumors and tumor burden per tumor-bearing rat were reduced and tumor latency was increased in all rats fed diets containing DFMO. Body weight gain, but not food intake, of rats fed the 20% fat + 0.5% DFMO diets was significantly less than in rats fed the 20% fat diets. Prostaglandin E and leukotriene (LTB4) syntheses, ODC activity and mammary tumorigenesis were significantly inhibited by feeding the diet containing menhaden oil or by adding 0.5% DFMO to any of the high fat diets. Feeding a 20% CO diet containing 0.004% INDO significantly reduced prostaglandin synthesis and ODC activity and increased LTB4 synthesis of mammary tumors but did not inhibit mammary tumorigenesis. This study suggests that the 5-lipoxygenase product LTB4

may be involved in mammary tumor production. Whereas a decrease in LTB4 appears to be associated with a decrease in tumorigenesis, an increase (as seen in the indomethacin group) was not associated with any change in the tumorigenic response.

L11 ANSWER 40 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
ACCESSION NUMBER: 1988:381212 BIOSIS
DOCUMENT NUMBER: BA86:65122
TITLE: AMIODARONE CAUSES ACUTE OXIDANT LUNG INJURY IN VENTILATED AND PERFUSED RABBIT LUNGS.
AUTHOR(S): KENNEDY T P; GORDON G B; PAKY A; MCSHANE A; ADKINSON N F JR; PETERS S P; FRIDAY K; JACKMAN W; SCIUTO A M; GURTNER G H
CORPORATE SOURCE: PULMONARY DIV., UNIV. TENNESSEE CENT. HEALTH SCIENCES, 956 COURT, ROOM H314, MEMPHIS, TENN. 38163.
SOURCE: J CARDIOVASC PHARMACOL, (1988) 12 (1), 23-36.
CODEN: JCPCDT. ISSN: 0160-2446.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Amiodarone (ADR), a new antiarrhythmic drug for life-threatening cardiac arrhythmias, causes pneumonitis or lung fibrosis in a sizeable minority of patients. The cause of lung damage is not known. We have shown that infusion of 10 mg amiodarone into the inflow circuit of ventilated and perfused rabbit lungs causes immediate increase in pulmonary artery pressure (mean ± SEM) (from 13.6 ± 1.2 to 40.6 ± 9.5 mm Hg, $p < 0.01$) and pulmonary edema with marked increase in the pulmonary generation of thromboxane and leukotrienes C4 and/or D4. Albumin (2 g%) in the perfusate prevents any increase in lung perfusion pressure or edema formation. When lung perfusion pressure increase is blocked with the combined cyclooxygenase and **lipoxygenase** inhibitor enolicam sodium (CG5391B, 35 μM in perfusate), significant lung edema still occurs after amiodarone, indicating that amiodarone causes increased alveolar-capillary membrane permeability. Addition of catalase (100 U/ml) or superoxide dismutase and catalase (100 U/ml each) to perfusate fails to protect from amiodarone lung injury. Immediate infusion of amiodarone (10 mg) into lungs ventilated with room air (ADR + RA) causes an increase in lung **weight gain** from baseline (ΔW) of 5.7 ± 1.5 g/min. Compared with ADR + RA, ventilation of lungs with 4% O2 (ΔW = 0.7 ± 0.3 g/min, $p < 0.05$), pretreatment of rabbits for 3 days with butylated hydroxyanisole (BHA, 100 mg/kg/day i.p., ΔW = 0.05 ± 0.02 g/min, $p < 0.01$), pretreatment of rabbits for 3 days with vitamin E (Vit E, 300 U/day orally, ΔW = 0.6 ± 0.2 g/min, $p < 0.05$), or addition of N-acetylcysteine to the lung perfusate (NAC, 5 mM, ΔW = 0.1 ± 0.08 g/min, $p < 0.01$) all protect from lung edema formation after amiodarone. Amiodarone (100 mg) also caused a marked increase in luminol-enhanced lung chemiluminescence, lung production of superoxide anion (O2-), and tissue levels of lung glutathione disulfide. These results suggest that amiodarone causes lung injury by an oxidant mechanism.

=> d ti 1-34

L11 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2002 ACS
TI Diagnosis of diabetes mellitus and insulin resistance by measuring the expression of genes associated with obesity

L11 ANSWER 2 OF 40 USPATFULL
TI Adhesive microsphere drug delivery composition

L11 ANSWER 3 OF 40 USPATFULL
TI Identification of molecular interaction sites in RNA for novel drug discovery

L11 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
TI Physiological response of Colorado potato beetle and beet armyworm larvae to depletion of wound-inducible proteinase inhibitors in transgenic potato plants

L11 ANSWER 5 OF 40 USPATFULL
TI Drug delivery device

L11 ANSWER 6 OF 40 USPATFULL

TI Hydroalcoholic compositions for transdermal penetration of pharmaceutical agents

L11 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2002 ACS
TI The expression of adipogenic genes is decreased in obesity and diabetes mellitus

L11 ANSWER 8 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Protection against the diabetogenic effect of feeding tert-butylhydroquinone to rats prior to the administration of streptozotocin.

L11 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2002 ACS
TI Augmented insulinotropic action of arachidonic acid through the **lipoxygenase** pathway in the **obese** Zucker rat

L11 ANSWER 10 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Benzofuranyl ureas with potent cardiovascular teratogenicity in rats.

L11 ANSWER 11 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Effects of soybean (Glycine max) germination on biologically active components, nutritional values of seeds, and biological characteristics in rats.

L11 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2002 ACS
TI Preparation of amidocarboxylic acid derivatives as inhibitors of aldose reductase, 5-lipoxygenase, and lipid peroxide formation and as peroxisome proliferator-activated receptor (PPAR) activators

L11 ANSWER 13 OF 40 USPATFULL
TI Hydroalcoholic compositions thickened using surfactant/polymer complexes

L11 ANSWER 14 OF 40 USPATFULL
TI Benzimidazole derivatives, their preparation and their therapeutic use

L11 ANSWER 15 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Quinolines attenuate PAF-induced pulmonary pressor responses and edema formation.

L11 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
TI Antisense-mediated depletion of a potato **lipoxygenase** reduces wound induction of proteinase inhibitors and increases **weight gain** of insect pests

L11 ANSWER 17 OF 40 USPATFULL
TI Transmucosal drug delivery device

L11 ANSWER 18 OF 40 USPATFULL
TI Bioadhesive composition and patch

L11 ANSWER 19 OF 40 USPATFULL
TI Bioadhesive composition and patch

L11 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
TI Decreased activity of arachidonate 12-lipoxygenase in platelets of Japanese patients with non-insulin-dependent diabetes mellitus

L11 ANSWER 21 OF 40 USPATFULL
TI Tumor necrosis factor production inhibitors

L11 ANSWER 22 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Dietary fish oil or lofrin, a 5-lipoxygenase inhibitor, decrease the growth-suppressing effects of coccidiosis in broiler chicks.

L11 ANSWER 23 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Attenuation of diet-induced atherosclerosis in rabbits with a highly selective 15-lipoxygenase inhibitor lacking significant antioxidant properties.

L11 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2002 ACS
TI Preparation of benzimidazolylalkoxyarenes for treatment of hyperlipemia, hyperglycemia, obesity, impaired glucose tolerance, insulin resistance, and diabetic complications.

L11 ANSWER 25 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Intratracheal administration of DBcAMP attenuates edema formation in

phosgene-induced acute lung injury.

L11 ANSWER 26 OF 40 USPATFULL
TI Tramsdermal drug delivery device

L11 ANSWER 27 OF 40 USPATFULL
TI Diphenylpyrrolylfuran derivatives

L11 ANSWER 28 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Intrinsic 5-lipoxygenase activity is required for neutrophil responsivity.

L11 ANSWER 29 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Inhibition of two-stage skin carcinogenesis as well as complete skin carcinogenesis by oral administration of RMK688, a potent lipoxygenase inhibitor.

L11 ANSWER 30 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Induced resistance in soybean to Helicoverpa zea: Role of plant protein quality.

L11 ANSWER 31 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Expression of desiccation-induced and lipoxygenase genes during the transition from the maturation to the germination phases in soybean somatic embryos.

L11 ANSWER 32 OF 40 USPATFULL
TI Transdermal drug delivery backing

L11 ANSWER 33 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI On the suppression of food intake in experimental models of colitis in the rat.

L11 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
TI Protection against platelet-activating factor-induced injury by interferon inducer in perfused rabbit lung

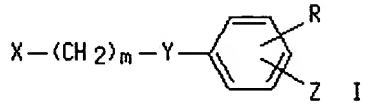
=> d ibib abs kwic 24, 23, 14, 12, 27, 28, 33, 32

L11 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2002 ACS
Full Text
ACCESSION NUMBER: 1997:56115 CAPLUS
DOCUMENT NUMBER: 126:104083
TITLE: Preparation of benzimidazolylalkoxyarenes for treatment of hyperlipemia, hyperglycemia, obesity, impaired glucose tolerance, insulin resistance, and diabetic complications.
INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru; Yanagisawa, Hiroaki; Fujimoto, Koichi; Fujiwara, Toshihiko; Horikoshi, Hiroyoshi; Yoshioka, Takao
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 227 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 745600	A1	19961204	EP 1996-303940	19960531
EP 745600	B1	20011024		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2177858	AA	19961202	CA 1996-2177858	19960531
NO 9602239	A	19961202	NO 1996-2239	19960531
ZA 9604518	A	19961209	ZA 1996-4518	19960531
AU 9654627	A1	19961212	AU 1996-54627	19960531
AU 712390	B2	19991104		
JP 09295970	A2	19971118	JP 1996-137930	19960531
JP 2976885	B2	19991110		
RU 2125048	C1	19990120	RU 1996-110410	19960531
TW 449594	B	20010811	TW 1996-85106495	19960531
AT 207489	E	20011115	AT 1996-303940	19960531
ES 2164841	T3	20020301	ES 1996-303940	19960531

CN 1157288	A	19970820	CN 1996-110937		19960601
CN 1066729	B	20010606			
JP 2000001487	A2	20000107	JP 1999-150312		19990528
JP 3249490	B2	20020121			
PRIORITY APPLN. INFO.:			JP 1995-135097	A	19950601
			JP 1996-45845	A	19960304
			JP 1996-137930	A3	19960531

OTHER SOURCE(S): MARPAT 126:104083
GI



I

AB Title compds. [I; X = (substituted) benzimidazolyl; Y = O, S; Z = 2,4-dioxothiazolidin-5-ylidenylmethyl, 2,4-dioxothiazolidin-5-ylmethyl, 2,4-dioxo-oxazolidin-5-ylmethyl, 3,5-dioxooxadiazolidin-2-ylmethyl, CH2N(OH)CONH2; R = H, alkyl, alkoxy, halo, OH, NO2, amino, aralkyl; m = 1-5], were prepd. Thus, N-methyl-1,2-phenylenediamine and 5-[4-(ethoxycarbonylmethoxy)benzyl]thiazolidine-2,4-dione (prepn. given) were refluxed 5 h in aq. HCl/dioxane to give 5-[4-(1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione. The latter at 5 μg/mL gave 80.3% inhibition of bovine lens aldose reductase.

IT 9028-31-3, Aldose reductase 80619-02-9, 5-**Lipoxygenase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; prepn. of benzimidazolylalkoxyarenes for treatment of hyperlipemia, hyperglycemia, **obesity**, impaired glucose tolerance, insulin resistance, and diabetic complications)

L11 ANSWER 23 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text

ACCESSION NUMBER:	1997:215877 BIOSIS
DOCUMENT NUMBER:	PREV199799522381
TITLE:	Attenuation of diet-induced atherosclerosis in rabbits with a highly selective 15-lipoxygenase inhibitor lacking significant antioxidant properties.
AUTHOR(S):	Sendobry, Sandra M.; Cornicelli, Joseph A.; Welch, Kathryn; Bocan, Thomas; Tait, Bradley; Trivedi, Bharat K.; Colbry, Norman; Dyer, Richard D.; Feinmark, Steven J.; Daugherty, Alan (1)
CORPORATE SOURCE:	(1) Cardiovasc. Div., Box 8086, Washington Univ. Sch. Med., 660 S. Euclid Ave., St. Louis, MO 63110 USA
SOURCE:	British Journal of Pharmacology, (1997) Vol. 120, No. 7, pp. 1199-1206. ISSN: 0007-1188.
DOCUMENT TYPE:	Article
LANGUAGE:	English

AB 1. 15-**Lipoxygenase** (15-LO) has been implicated in the pathogenesis of atherosclerosis because of its localization in lesions and the many biological activities exhibited by its products. To provide further evidence for a role of 15-LO, the effects of PD 146176 on the development of atherosclerosis in cholesterol-fed rabbits were assessed. This novel drug is a specific inhibitor of the enzyme in vitro and lacks significant non specific antioxidant properties. 2. PD 146176 inhibited rabbit reticulocyte 15-LO through a mixed noncompetitive mode with a K-i of 197 nM. The drug had minimal effects on either copper or 2,2'-azobis(2-amidinopropane)hydrochloride (ABAP) induced oxidation of LDL except at concentrations 2 orders higher than the K-i. 3. Control New Zealand rabbits were fed a high-fat diet containing 0.25% wt./wt. cholesterol; treated animals received inhibitor in this diet (175 mg kg-1, b.i.d.). Plasma concentrations of inhibitor were similar to the estimated K-i (197 nM). During the 12 week study, there were no significant differences in **weight gain**, haematocrit, plasma total cholesterol concentrations, or distribution of lipoprotein cholesterol. 4. The drug plasma concentrations achieved in vivo did not inhibit low-density lipoprotein (LDL) oxidation in vitro. Furthermore, LDL isolated from PD 146176-treated animals was as susceptible as that from controls to oxidation ex vivo by either copper or ABAP. 5. PD 146176 was very effective in suppressing atherogenesis, especially in the aortic arch where lesion coverage diminished from 15 +-

4 to 0% (P lt 0.02); esterified cholesterol content was reduced from 2.1 +- 0.7 to 0 mu-g mg-1 (P lt 0.02) in this region. Immunostainable lipid-laden macrophages present in aortic intima of control animals were totally absent in the drug-treated group. 6. Results of these studies are consistent with a role for 15-LO in atherogenesis.

L11 ANSWER 14 OF 40 USPATFULL
Full Text

ACCESSION NUMBER:	1999:37128 USPATFULL
TITLE:	Benzimidazole derivatives, their preparation and their therapeutic use
INVENTOR(S):	Fujita, Takashi, Tokyo, Japan Wada, Kunio, Tokyo, Japan Oguchi, Minoru, Tokyo, Japan Yanagisawa, Hiroaki, Tokyo, Japan Fujimoto, Koichi, Tokyo, Japan Fujiwara, Toshihiko, Tokyo, Japan Horikoshi, Hiroyoshi, Tokyo, Japan Yoshioka, Takao, Tokyo, Japan
PATENT ASSIGNEE(S):	Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5886014		19990323	
APPLICATION INFO.:	US 1996-657041		19960531	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1995-45845	19950601
	JP 1995-135097	19950601

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Shah, Mukund J.
ASSISTANT EXAMINER:	Ngo, Tamthom T.
LEGAL REPRESENTATIVE:	Frishauf, Holtz, Goodman, Langer & Chick, P.C.
NUMBER OF CLAIMS:	116
EXEMPLARY CLAIM:	1
LINE COUNT:	4949

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula (I): ##STR1## [wherein: X represents an optionally substituted benzimidazole group; Y represents an oxygen or sulfur atom; Z represents a 2,4-dioxothiazolidin-5-ylidenylmethyl, 2,4-dioxothiazolidin-5-ylmethyl, 2,4-dioxooxazolidin-5-ylmethyl, 3,5-dioxooxadiazolidin-2-ylmethyl or N-hydroxyureidomethlyl group; R represents hydrogen, alkyl, alkoxy, halogen, hydroxy, nitro, amino or aralkyl; and m is an integer from 1 to 5]; have valuable activity for the treatment and/or prophylaxis of a variety of disorders, including one or more of: hyperlipemia, hyperglycemia, obesity, impaired glucose tolerance (IGT), insulin resistance and diabetic complications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The compounds of formula (I) and salts thereof possess the ability to reduce insulin resistance, hyperlipidemia, hyperglycemia, gestational diabetes mellitus, **obesity**, impaired glucose tolerance, diabetic complications, arteriosclerosis, cataracts, and polycystic ovary syndrome, and, in addition, have aldose reductase inhibitory activity, 5-**lipoxygenase** inhibitory activity and the ability to inhibit the formation of lipid peroxide. They are thus useful for the prevention and/or therapy of hyperlipidemia, hyperglycemia, **obesity**, impaired glucose tolerance, hypertension, osteoporosis, cachexia, fatty liver, diabetic complications, arteriosclerosis, and cataracts; for the prevention and/or therapy of other. . .

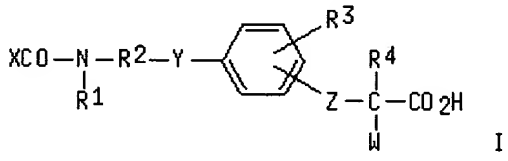
CLM What is claimed is:
32. A pharmaceutical composition for the treatment or prophylaxis of insulin resistance, diabetes, hyperglycemia, arteriosclerosis, cataracts, hyperlipemia, **obesity**, impaired glucose tolerance, hypertension, polycystic ovary syndrome, gestational diabetes mellitus or insulin resistant non-IGT, and complications thereof, or for the inhibition of aldose reductase, 5-**lipoxygenase** or lipid peroxide, and complications thereof, which composition comprises an effective amount of an active compound in admixture with a. . .

L11 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2002 ACS
Full Text

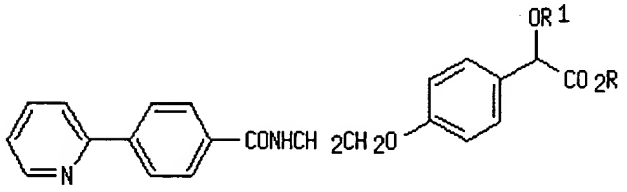
ACCESSION NUMBER: 1999:244628 CAPLUS
DOCUMENT NUMBER: 130:296612
TITLE: Preparation of amidocarboxylic acid derivatives as inhibitors of aldose reductase, 5-lipoxygenase, and lipid peroxide formation and as peroxisome proliferator-activated receptor (PPAR) activators
INVENTOR(S): Yanagisawa, Hiroaki; Sakurai, Mitsuya; Takamura, Makoto; Fujiwara, Toshihiko
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 720 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918066	A1	19990415	WO 1998-JP4396	19980930
W: AU, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RU, TR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2305808	AA	19990415	CA 1998-2305808	19980930
AU 9892798	A1	19990427	AU 1998-92798	19980930
AU 738134	B2	20010906		
EP 1026149	A1	20000809	EP 1998-945527	19980930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9813019	A	20000905	BR 1998-13019	19980930
NO 2000001689	A	20000531	NO 2000-1689	20000331

PRIORITY APPLN. INFO.: JP 1997-269923 A 19971002
WO 1998-JP4396 W 19980930
OTHER SOURCE(S): MARPAT 130:296612
GI



I



II

AB Claimed and prepd. are amidocarboxylic acid derivs. (phenylalkanoic acids contg. arylcarboxamide derivs.) represented by general formula (I), pharmacol. acceptable salts thereof, or pharmacol. acceptable esters thereof, [wherein R1 = H, linear or branched C1-6 alkyl, C7-12 aralkyl; R2 = linear or branched C1-6 alkylene; R3 = H, linear or branched alkyl C1-6 alkyl, C1-4 alkoxy, or C1-4 alkylthio, halo, NO2, di(linear or branched C1-4 alkyl)amino, (un)substituted C6-10 aryl, C7-12 aralkyl optionally having 1-5 substituents on the aryl, OH, linear or branched C1-5 aliph. acyl; R4 = H, linear or branched C1-6 alkyl; Z = linear or branched C1-6 alkylene; W = HO, linear or branched C1-6 alkyl, C1-4 alkoxy, or C1-4 alkylthio, (un)substituted C6-10 aryl, C6-10 aryloxy, C6-10 arylthio, C7-12 aralkyloxy, C7-12 aralkylthio, or C6-10 aryloxy-linear or branched C1-4 alkyl each optionally having 1-5 substituents on the aryl, 5- to 10-membered mono- or bicyclic heteroaryloxy contg. 1-4 heteroatoms selected from O, N, and S, etc.; X = C6-10 aryl optionally having 1-3 substituents, 5- to 10-membered mono- or bicyclic heteroaryl contg. 1-4

heteroatoms selected from O, N, and S; Y = single bond, O, S, (un)substituted NH]. Also claimed are blood sugar- and blood lipid-lowering agents, insulin resistance improver, antiinflammatory agents, immunomodulators, aldose reductase inhibitors, 5-**lipoxygenase** inhibitors, lipid peroxide formation inhibitors, PPAR activators, and anti-osteoporosis agents and therapeutic or prophylactic agents for diabetes, hyperlipemia, **obesity**, impaired glucose tolerance, insulin resistant non-impaired glucose tolerance, fatty liver, diabetes complications, gestational diabetes mellitus, polycystic ovary syndrome, osteoarthritis, rheumatoid arthritis, allergies, asthma, cancers, autoimmune diseases, pancreatitis, and cataract. Thus, N-deprotection of Et 2-ethoxy-3-[4-(2-phthalimidoethoxy)phenyl]propionate with hydrazine hydrate in MeOH at room temp. for 1.5 h followed by amidation with 4-pyridin-2-ylbenzoic acid using carbonyl diimidazole in CH2Cl2 at room temp. for 1. 5 h followed by sapon. with a mixt. of 1 N aq. NaOH and MeOH and acidification gave 3-[4-[2-(4-pyridin-2-ylbenzoylamino)ethoxy]phenyl]propionic acid deriv. (II.Na; R = H, R1 = Et) (III). III and (S)-II (R = H, R1 = 4-isopropoxyphenyl) in feed contg. 0.01% at ~10 mg drug/kg/day for 3 days lowered blood sugar level by 43 and 73%, resp. A capsule, a tablet, and a granule formulation contg. III were prepd.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Allergy inhibitors
Anti-inflammatory agents
Antiasthmatics
Antidiabetic agents
Antiobesity agents
Antitumor agents
Autoimmune disease
Cataract
Hypoglycemia
Hypolipemic agents
Immunomodulators
Osteoarthritis
Osteoporosis
Rheumatoid arthritis
(prepn. of amidocarboxylic acid derivs. as inhibitors of aldose reductase, 5-**lipoxygenase**, and lipid peroxide formation and as peroxisome proliferator-activated receptor (PPAR) activators for treatment and prevention of diseases)

L11 ANSWER 27 OF 40 USPATFULL
Full Text

ACCESSION NUMBER:	94:51428 USPATFULL
TITLE:	Diphenylpyrrolylfuran derivatives
INVENTOR(S):	Adachi, Jun, Namerikawa, Japan Ishida, Mitsugu, Namerikawa, Japan Taniguchi, Toshietsu, Namerikawa, Japan Kato, Yuichi, Namerikawa, Japan Kawagoshi, Toshiyuki, Namerikawa, Japan Tamura, Tomoaki, Namerikawa, Japan Kadozaki, Tetsuo, Namerikawa, Japan Miyamoto, Tetsuo, Namerikawa, Japan
PATENT ASSIGNEE(S):	Nihon Iyakuhin Kogyo Co., Ltd., Toyama, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5321041		19940614	
APPLICATION INFO.:	US 1993-140514		19931025	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1992-286250	19921023

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Lee, Mary C.
ASSISTANT EXAMINER:	McKane, Joseph K.
LEGAL REPRESENTATIVE:	Cushman, Darby & Cushman
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
LINE COUNT:	1266

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Diphenylpyrrolylfuran derivatives represented by the following formula (I): ##STR1## wherein R1 and R2 may be the same or different

and independently represent a hydrogen atom, a halogen atom, a lower alkyl group, a lower alkoxy group, a lower alkylthio group, or a lower alkylsulfenyl group; m and n independently represent an integer of from 1 to 3; R3 represents a hydrogen atom or a lower alkyl group, R4 represents a hydrogen atom, a lower alkyl group, or a lower acyl group; and R5 represents a hydrogen atom, a lower alkyl group which may have one or more suitable substituents, a lower alkoxy- or an aryloxy-carbonyl group, an acyl group, or a sufonyl group, and pharmaceutically acceptable salts thereof are disclosed. The compounds disclosed are useful as anti-inflammatory agent, anti-allergic agents, anti-platelet agents and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . invention and the salts thereof are useful since they have pharmacological effects such as inhibitory activities on lipid peroxidation, cyclooxygenase, 5-**lipoxygenase**, carrageenin-induced paw edema, granuloma formation and platelet aggregation. The compounds of the formula (I) are particularly useful since they exhibit dual inhibition against cyclooxygenase and 5-**lipoxygenase**, each of them is a key enzyme in the arachidonic acid metabolic pathway. On the basis of these activities, the. . . hyperlipidemia, diabetic angiopathy, arterio sclerosis, peptic ulcer, alcoholic hepatitis, cirrhosis, fatty liver, cancer, side effects of anti-cancer agent, retinopathy, cataract, **obesity**, gestosis, radiation injury, shock, sepsis and various senile regressive diseases.

L11 ANSWER 28 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
ACCESSION NUMBER: 1994:442827 BIOSIS
DOCUMENT NUMBER: PREV199497455827
TITLE: Intrinsic 5-lipoxygenase activity is required for neutrophil responsivity.
AUTHOR(S): Guidot, David M. (1); Repine, Michael J.; Westcott, Jay Y.; Repine, John E.
CORPORATE SOURCE: (1) Webb-Waring Inst. Biomed. Res., Dep. Med., Univ. Colo. Health Sci. Cent., 4200 East Ninth Ave., Box C-321, Denver, CO 80262 USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) Vol. 91, No. 17, pp. 8156-8159.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English

AB We found that intrinsic neutrophil 5-**lipoxygenase** activity was necessary for human neutrophil adherence and chemotaxis in vitro and human neutrophil-mediated acute edematous injury in isolated perfused rat lungs given interleukin 8 intratracheally. Treatment with either Zileuton (a specific reversible competitive inhibitor of 5-**lipoxygenase**) or MK886 (a specific irreversible inhibitor of the 5-**lipoxygenase** activator protein) prevented stimulated neutrophil adherence and chemotaxis (but not superoxide anion production) in vitro. Zileuton- or MK886-inhibited neutrophil chemotaxis was not restored by adding leukotriene B-4 in vitro. Perfusion with neutrophils and either Zileuton or MK886, or with MK886-pretreated neutrophils (without adding MK886 to the perfusate), also prevented lung injury (reflected by lung **weight gain** and lung Ficoll retention) and perfusate leukotriene B-4 increases in isolated rat lungs given interleukin 8 intratracheally. Again, adding leukotriene B-4 to the perfusate did not damage interleukin 8-treated isolated lungs perfused with Zileuton-inhibited neutrophils. We conclude that intrinsic 5-**lipoxygenase** activity is required for neutrophil adherence and chemotaxis and neutrophil-mediated lung injury.

L11 ANSWER 33 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
Full Text
ACCESSION NUMBER: 1993:317775 BIOSIS
DOCUMENT NUMBER: PREV199396026125
TITLE: On the suppression of food intake in experimental models of colitis in the rat.
AUTHOR(S): McHugh, K. J.; Weingarten, H. P.; Keenan, C.; Wallace, J. L.; Collins, S. M. (1)
CORPORATE SOURCE: (1) Intestinal Dis. Res. Unit, Room 3N5c, McMaster Univ. Med. Cent., Hamilton, ON L8N 3Z5 Canada
SOURCE: American Journal of Physiology, (1993) Vol. 264, No. 5 PART 2, pp. R871-R876.
ISSN: 0002-9513.

DOCUMENT TYPE: Article
LANGUAGE: English
AB We measured daily food intake and body weight in rats before and after the induction of colitis by intrarectal administration of either 2,4,6-trinitrobenzenesulfonic acid in ethyl alcohol (TNBE) or 4% acetic acid (AA). Administration of TNBE or AA induced inflammation in the distal colon, which was reflected by a significant increase in myeloperoxidase (MPO) activity in the colon. On days 1, 2, and 3 after induction of colitis by TNBE, food intake fell by 80, 70, and 50%, respectively, compared with pretreatment values; food intake returned to normal by day 4. Body weight fell within 24 h after induction of colitis and remained 10% less than control for at least 5 days. Colitis induced by AA produced a similar pattern and degree of decreased food intake and **weight loss**. Treatment with the 5'-**lipoxygenase** inhibitor MK-886 significantly reduced concentrations of leukotriene B-4 in the colon of TNBE-treated rats but did not affect food intake. In contrast, the cyclooxygenase inhibitor indomethacin decreased prostaglandin E-2 concentrations in the colon but also attenuated the suppression of feeding by 52 and 64% on the first 2 days after induction of colitis by TNBE. These results identify a specific prostaglandin-mediated suppression of feeding in the rat with acute colitis induced by TNBE and illustrate the utility of this model for studying mechanisms underlying anorexia associated with inflammation of the gastrointestinal tract.

L11 ANSWER 32 OF 40 USPATFULL
Full Text
ACCESSION NUMBER: 93:98163 USPATFULL
TITLE: Transdermal drug delivery backing
INVENTOR(S): Godbey, Kristin J., Ramsey, MN, United States
Martin, Philip G., Ramsey, MN, United States
PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Company, St. Paul, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5264219		19931123	
APPLICATION INFO.:	US 1992-926910		19920807	(7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Horne, Leon R.
LEGAL REPRESENTATIVE: Griswold, Gary L., Kirn, Walter N., Reedich, Douglas E.
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
LINE COUNT: 472
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polymer blends containing a very low density polyethylene copolymer of ethylene and 1-butene, 1-hexene, or 1-octene and about 15 to about 600 parts by weight of a linear low density polyethylene copolymer of ethylene and 1-octene, based on 100 parts by weight of the very low density polyethylene copolymer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . blockers (e.g., nifedipine, diltiazem); bronchodilators (e.g., theophylline, pirbuterol, salmeterol, isoproterenol); enzyme inhibitors such as collagenase inhibitors, protease inhibitors, elastase inhibitors, **lipoxygenase** inhibitors (e.g., A64077), and angiotensin converting enzyme inhibitors (e.g., captopril, lisinopril); other antihypertensives (e.g., propranolol); leukotriene antagonists (e.g., ICI204,219); anti-ulceratives. . . sumatripan); antiarrhythmic agents (e.g., flecainide); antiemetics (e.g., metaclopromide, ondansetron); anticancer agents (e.g., methotrexate); neurologic agents such as anxiolytic drugs; hemostatics; anti-**obesity** agents; and the like, as well as pharmaceutically acceptable salts and esters thereof. The amount of drug that constitutes a. . .